Exhibit B

~~IN THE~~ UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NATERA, INC.,

Plaintiff / Counterclaim-Defendant,

v.

ARCHERDX, INC., ARCHERDX, LLC, INVITAE CORPORATION

Defendants / Counterclaimants.

C.A. No. 20-125-LPS

JURY TRIAL DEMANDED

DEFENDANTS INVITAE CORPORATION'S AND ARCHERDX, LLC'S FIRST AMENDED ANSWER~~-~~ AND COUNTERCLAIMS TO PLAINTIFF'S SECOND AMENDED COMPLAINT FOR PATENT INFRINGEMENT

Defendants Invitae Corporation ("Invitae") and ArcherDX, LLC ("ArcherDX") (collectively, "Defendants") hereby submit the following preliminary statement, answer, defenses (affirmative and otherwise), and counterclaims to Natera, Inc.'s ("Natera" or "Plaintiff") Second Amended Complaint (D.I. 116) filed on January 12, 2021.

PRELIMINARY STATEMENT

a. Invitae is a leading medical genetics company whose mission is to bring comprehensive genetic information into mainstream medicine to improve healthcare for billions of people. Invitae's goal is to aggregate the world's genetic tests into a single service with higher quality, faster turnaround time, and lower prices.

b. ArcherDX is a leading genomics company democratizing precision oncology, including the use of genetic information from genomic tumor profiling to guide cancer therapy optimization and monitoring. ArcherDX offers a suite of innovative products and services that are highly accurate, personal, actionable, and easy to use in local settings.

c. With its proprietary product development platform, ArcherDX is developing

industry-leading products and services to optimize therapy and monitor cancer. Specifically, ArcherDX is in the process of developing *in vitro* diagnostic ("IVD") products for approval or clearance by the United States Food and Drug Administration ("FDA"). For example, STRATAFIDE™ is in development as a universal IVD and companion diagnostic product. STRATAFIDE™ has twice received Breakthrough Device designation from the FDA. In January 2020, ArcherDX also received Breakthrough Device designation from the FDA for its Personalized Cancer Monitoring product, PCM, which it is developing as an IVD to non-invasively and quantitatively measure cancer recurrence or progression, as well as therapeutic efficacy.

d. Natera's U.S. Patent Nos. 10,538,814 ("the '814 Patent"), 10,557,172 ("the '172 patent"), 10,590,482 ("the '482 patent") (collectively, "the Asserted cfDNA Patents"), 10,597,708 ("the '708 patent"), and 10,731,220 ("the '220 patent") (together with the Asserted cfDNA Patents, the "Asserted Patents") stem from protracted and convoluted prosecutions at the U.S. Patent and Trademark Office ("USPTO"). Over the course of a decade, Natera filed a plethora of provisional, continuation, and continuation-in-part patent applications, and it abandoned many of them. In connection with those applications, Natera filed *hundreds* of proposed claims with the USPTO and disclosed *thousands* of references. But Natera did not disclose key prior art that discloses or renders obvious the claimed methods for amplifying and sequencing nucleic acids.

e. Moreover, despite this protracted and convoluted prosecution history, prior to April 30, 2019, when it filed the applications that resulted in the Asserted Patents, Natera had *never* disclosed nor sought to patent the methods recited in the claims of the Asserted Patents. Indeed, that is because Natera did not invent those methods; tellingly, Natera does not allege in its Second Amended Complaint that it even practices the methods claimed in the Asserted Patents.

f. Instead, on information and belief, Natera is a copyist that drafted claims designed to cover ArcherDX's proprietary Anchored Multiplex PCR ("AMP™") processes—after being outcompeted in the marketplace; ArcherDX's proprietary AMP™ processes are technologically and commercially superior to Natera's legacy technology.

g. Notably, Natera filed the applications leading to the Asserted Patents shortly after it gained access to confidential information relating to ArcherDX's products, including LIQUIDPlex™, STRATAFIDE™, and PCM.

h. As described below, Natera's efforts to stymie ArcherDX's technological advantage violate the patent laws on multiple levels: the belatedly drafted claims fail to satisfy the substantive requirements of patentability, including 35 U.S.C. §§ 101, 102, 103, and/or 112; no one associated with Natera invented the claimed methods; and Natera's unreasonable delay in prosecution—coupled with its filings of the applications leading to the Asserted Patents soon after it gained access to ArcherDX's confidential information and for the purpose of attempting to unjustifiably regain traction in the marketplace—trigger the doctrines of unclean hands and prosecution laches, barring Natera's infringement claims.

i. In any event, Natera is a poor copyist. The Defendants do not practice the technology claimed in any of the Asserted Patents, and therefore does not infringe. Moreover, activities complained of by Natera are protected by the safe harbor of 35 U.S.C. § 271(e)(1) and, accordingly, immune from infringement claims.

j. In an attempt to harass and cast a cloud over ArcherDX, Natera improperly seeks a preliminary and inappropriate advisory opinion from the Court regarding ArcherDX's STRATAFIDE™ and PCM products, which are still in the development stage—without an application for FDA approval even on file.

k. Finally, Natera moved to add Invitae as a party to its Second Amended Complaint in its attempt to cast a wide net of blame, even though Invitae did not develop the accused products.

l. In sum, Natera's meritless Second Amended Complaint represents a last-ditch effort to bully a smaller, technologically advanced company using the courtroom, because Natera fears it will be unable to succeed with its inferior products in the marketplace.

ANSWER

The Defendants deny all allegations in the Second Amended Complaint, whether express or implied, that are not specifically admitted below, including all allegations in any headings or unnumbered paragraphs. The Defendants further deny that Natera is entitled to the requested relief or any other relief.

OVERVIEW OF THE ACTION[1]

1. The Defendants expressly deny that any ArcherDX product falls within the alleged scope of any claim of the '814 Patent, the '172 Patent, the '482 Patent, the '708 Patent, and the '220 patent, and that any of its activities constitute "infringement of Natera's innovative, patented technology." The Defendants admit that the Second Amended Complaint purports to state an action for infringement of the '814 Patent, the '172 Patent, the '482 Patent, the '708 Patent, and the '220 Patent. The Defendants admit that LIQUIDPlex™ was previously called Reveal ctDNA. LIQUIDPlex™ is a product sold for research use only, and it uses ArcherDX's proprietary AMP™ chemistry. FusionPlex® and VariantPlex® are also products sold for research use only, and use ArcherDX's proprietary AMP™ chemistry. Besides LIQUIDPlex™,

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1 For the Court's convenience, the Defendants generally adopt the headings used in Natera's Second Amended Complaint. In so doing, the Defendants do not admit that the headings are accurate, and reserves the right to contest any statement or characterization set forth under them. To the extent the headings constitute allegations requiring a response, they are denied.

FusionPlex® and VariantPlex®, ArcherDX does not sell, or have in development, any other products for research use only that use ArcherDX's proprietary AMP™ chemistry. The Defendants further admit that ArcherDX is currently developing its STRATAFIDE™ and PCM products for approval or clearance by the FDA. The Defendants further admit that Archer®MET is an IVD product that has been approved in Japan only. The Defendants deny the allegation that ArcherDX "does not have freedom to operate its AMP products for minimal residual disease ("MRD") and personalized cancer monitoring." The Defendants further deny each and every allegation of paragraph 1 of the Second Amended Complaint.

THE PARTIES

2. The Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 2 of the Second Amended Complaint, and therefore denies each and every allegation in that paragraph.

3. Paragraph 3 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 3 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

4. Paragraph 4 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 4 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

5. Paragraph 5 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 5 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

6. Paragraph 6 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 6 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

7. Paragraph 7 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 7 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

8. Paragraph 8 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 8 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

9. The Defendants deny the allegations of paragraph 9 of the Second Amended Complaint. The Defendants specifically deny that ArcherDX has committed the alleged acts of infringement and further denies that any Asserted Patent claims an "invention." The Defendants aver that all Asserted Patents are invalid for failure to satisfy one or more conditions for patentability set forth under 35 U.S.C. including but not limited to §§ 101, 102, 103, and 112 et seq.; no one associated with Natera invented the claimed methods; and the Asserted Patents are unenforceable against the Defendants by reason of Natera's unclean hands and prosecution laches.

10. ArcherDX admits that ArcherDX, Inc. was, at the time of the filing of this action, a corporation organized and existing under the laws of the State of Delaware, having a place of business at 2477 55th Street, Suite 202, Boulder, Colorado 80301. ArcherDX admits that

ArcherDX, LLC is a limited liability company, organized and existing under the laws of the State of Delaware.

11. Invitae admits that it is a corporation organized and existing under the laws of the States of Delaware, having a principal place of business at 1400 16th Street, San Francisco, CA 94103.

12. The Defendants admit that Invitae's Form 8-K, filed on October 5, 2020, indicates that on October 2, 2020, Invitae consummated the acquisition of ArcherDX, Inc., from which ArcherDX, LLC became a wholly-owned subsidiary of Invitae.

13. The Defendants admit that it represented that effective October 2, 2020, Defendant ArcherDX Inc. merged with Apollo Merger Sub A Inc., which then merged with Apollo Merger Sub B LLC to form ArcherDX, LLC (referenced herein as "ArcherDX"). The Defendants admit that the Court has substituted ArcherDX, LLC for ArcherDX, Inc.

14. Paragraph 14 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent paragraph 14 excerpts the contents of an Invitae document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is required, ArcherDX denies each and every allegation in paragraph 14 of the Second Amended Complaint.

15. The Defendants deny the allegations of paragraph 15 of the Second Amended Complaint. ArcherDX independently developed its own proprietary AMP™ chemistry, technology platform, and applications, which are covered by three issued patents and 15 pending patent applications in the United States and two issued patents and 43 pending patent applications in foreign countries.

JURISDICTION AND VENUE

16. The allegation of jurisdiction in paragraph 16 of the Second Amended Complaint constitutes a legal conclusion that requires no response. To the extent a response is required, the Defendants admit that the Second Amended Complaint purports to state an action that arises under the patent laws of the United States, 35 U.S.C. § 1, et seq. The Defendants specifically deny that the Second Amended Complaint states a claim upon which relief may be granted.

17. The allegation of jurisdiction in paragraph 17 of the Second Amended Complaint constitutes a legal conclusion that requires no response. To the extent a response is required, the Defendants admit that the Second Amended Complaint purports to state an action that arises under 28 U.S.C. §§ 1331 and 1338(a), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. The Defendants specifically deny that the Second Amended Complaint states a claim upon which relief may be granted. The Defendants further deny that the Second Amended Complaint pleads the existence of a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act with respect to ArcherDX's yet-to-be-FDA-approved IVD products (or any other oncology product in development or used overseas, and that utilizes the same technology as any of the Accused Products). Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 16.

18. The allegation of jurisdiction in paragraph 18 of the Second Amended Complaint constitutes a legal conclusion that requires no response. To the extent a response is required, the Defendants do not contest that this Court has personal jurisdiction over the Defendants for purposes of this action. ArcherDX admits that ArcherDx, Inc. was, at the time of the filing of this action, a corporation organized and existing under the laws of the State of Delaware, having a place of business at 2477 55th Street, Suite 202, Boulder, Colorado 80301. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 18.

19. The allegation of jurisdiction in paragraph 19 of the Second Amended Complaint constitutes a legal conclusion that requires no response. To the extent a response is required, the Defendants do not contest that this Court has personal jurisdiction over ArcherDX for purposes of this action. The Defendants specifically deny that ArcherDX has committed the alleged acts of infringement in this District or anywhere else. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 19.

20. The allegation of jurisdiction in paragraph 20 of the Second Amended Complaint constitutes a legal conclusion that requires no response. To the extent a response is required, the Defendants do not contest that this Court has personal jurisdiction over ArcherDX for purposes of this action. ArcherDX admits that it initiated the civil action *ArcherDX, Inc. et al v. Qiagen Sciences, LLC et al.*, 18-1019-MN (D. Del. 2018). Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 20.

21. The allegation of jurisdiction in paragraph 21 of the Second Amended Complaint constitutes a legal conclusion that requires no response. To the extent a response is required, the Defendants do not contest that this Court has personal jurisdiction over Invitae for purposes of this action. The Defendants specifically deny that Invitae has committed the alleged acts of infringement in this District or anywhere else. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 19.

22. The allegation of jurisdiction in paragraph 22 of the Second Amended Complaint constitutes a legal conclusion that requires no response. To the extent a response is required, the Defendants do not contest that this Court has personal jurisdiction over ArcherDX for purposes of this action. ArcherDX admits that ArcherDX, Inc. was, at the time of the filing of the action, a corporation organized and existing under the laws of the State of Delaware, having a place of

business at 2477 55th Street, Suite 202, Boulder, Colorado 80301. The Defendants do not contest that this Court has personal jurisdiction over Invitae for the purposes of this action. Invitae admits that it is a corporation organized and existing under the laws of the State of Delaware. Except as expressly admitted herein, ArcherDX denies each and every allegation of paragraph 22.

23. The allegation of jurisdiction in paragraph 23 of the Second Amended Complaint constitutes a legal conclusion that requires no response. To the extent a response is required, the Defendants do not contest that this Court has personal jurisdiction over Invitae for the purposes of this action. The Defendants specifically deny that the Defendants have committed the alleged acts of infringement in this District or anywhere else and also deny that Invitae is vicariously liable for any alleged infringing acts. The Defendants expressly deny that Invitae is the alter ego of ArcherDX. To the extent paragraph 23 excerpts the contents of an Invitae document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 23.

24. The Defendants admit that Natera accurately quoted Invitae's Form S-4 filed with the Securities and Exchange Commission on August 25, 2020. Except as expressly admitted herein, ArcherDX denies each and every allegation of paragraph 24.

25. The Defendants admit that Natera correctly quoted the prospectus for the merger. The Defendants deny that the emphasis indicated in the quoted language is accurate. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 25.

26. The Defendants deny that a "10-02-2020 Form 8-K" issued by Invitae exists as alleged. To the extent Natera intended to indicate Invitae's Form 8-K filed on a different date, the Defendants reserve the right to respond to any modification or clarification. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 26.

27. The Defendants admit that the web address https://archerdx.com/ displays ArcherDX's and Invitae" names and logos, states that "The Invitae-ArcherDX combination has now closed" and "We're Right Where You Need Us." Any other statements in paragraph 27 of the Second Amended Complaint contains statements of opinion to which no response is required. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 27.

28. The Defendants admit that the article cited by Natera is accurately quoted in paragraph 28. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 28.

29. The Defendants admit that Jason Myers, former CEO of ArcherDX, Inc., currently serves as Invitae's President of Oncology and sits on the Invitae Board of Directors. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 29.

30. The allegation of venue in paragraph 30 of the Second Amended Complaint constitutes a legal conclusion that requires no response. To the extent a response is required, the Defendants do not contest that, for the purposes of this action, and without waiving any defense of improper venue in connection with any other cause of action or claim, venue properly lies in this judicial district pursuant to 28 U.S.C. § 1400(b). The Defendants admit that ArcherDX, Inc. is a Delaware corporation. Except as expressly admitted herein, the Defendants further deny each and every allegation of paragraph 30.

31. The allegation of venue in paragraph 30 of the Second Amended Complaint constitutes a legal conclusion that requires no response. To the extent a response is required, the Defendants do not contest that, for the purposes of this action, and without waiving any defense of improper venue in connection with any other cause of action or claim, venue properly lies in

this judicial district pursuant to 28 U.S.C. § 1400(b). The Defendants admit that Invitae is a Delaware corporation. Except as expressly admitted herein, the Defendants further deny each and every allegation of paragraph 31.

BACKGROUND

32. Paragraph 32 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 32 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore deny each and every allegation in that paragraph.

33. Paragraph 33 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 33 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore deny each and every allegation in that paragraph.

34. Paragraph 34 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 34 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore deny each and every allegation in that paragraph.

35. Paragraph 35 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 35 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations, and therefore deny each and every allegation in that paragraph.

36. Paragraph 36 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 36 contains factual allegations, Natera does not identify any particular "MRD assessment" in paragraph 36, and accordingly the

Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore deny each and every allegation in that paragraph.

37. Paragraph 37 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 37 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore deny each and every allegation in that paragraph.

38. Paragraph 38 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 38 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore deny each and every allegation in that paragraph.

39. Paragraph 39 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 39 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations, and therefore deny each and every allegation in that paragraph.

40. Paragraph 40 of the Second Amended Complaint contains statements of opinion to which no response is required. To the extent paragraph 40 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore deny each and every allegation in that paragraph.

41. The Defendants deny that the Asserted Patents relate to "innovative new methods for amplifying and sequencing nucleic acids, including cell-free DNA." The Defendants further denies that the claims of the Asserted Patents recite methods that are novel or innovative. The Defendants aver that all Asserted Patents are invalid for failure to satisfy one or more conditions for patentability set forth under 35 U.S.C. including but not limited to §§ 101, 102, 103, and 112

et seq.; no one associated with Natera invented the claimed methods; and the Asserted Patents are unenforceable against the Defendants by reason of Natera's unclean hands and prosecution laches. Except as expressly denied herein, the Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 41 of the Second Amended Complaint, and therefore deny each and every allegation in that paragraph.

GENERAL BACKGROUND OF THE ASSERTED PATENTS

42. The Defendants admit that a document purporting to be a copy of the '814 Patent is attached to the Second Amended Complaint as Exhibit 1. The Defendants admit that, on its face, the '814 Patent, titled "Methods for Simultaneous Amplification of Target Loci," indicates that it was issued by the USPTO on January 21, 2020. As to the remaining allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 42 of the Second Amended Complaint, and therefore deny each and every allegation of that paragraph.

43. The Defendants admit that claim 1 of the '814 Patent recites:

> A method for amplifying and sequencing DNA, comprising:
>
> ligating adaptors to cell-free DNA isolated from a biological sample, wherein the adaptors each comprises a universal priming site;
>
> performing a first PCR to simultaneously amplify at least 10 target loci using a universal primer and at least 10 target-specific primers in a single reaction volume;
>
> performing a second, nested PCR to simultaneously amplify the at least 10 target loci using the universal primer and at least 10 inner target-specific primers in a single reaction volume, wherein at least one of the primers comprises a sequencing tag;
>
> performing high-throughput sequencing to sequence the amplified DNA comprising the target loci.

The Defendants admit that claim 1 recites a "method for amplifying and sequencing DNA" and further recites "PCR" and "high-throughput sequencing." Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 43 of the Second Amended Complaint.

44. The Defendants admit that a document purporting to be a copy of the '172 Patent is attached to the Second Amended Complaint as Exhibit 2. The Defendants admit that, on its face, the '172 Patent, titled "Methods for Simultaneous Amplification of Target Loci," indicates that it was issued by the USPTO on February 11, 2020. As to the remaining allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 44 of the Second Amended Complaint, and therefore deny each and every allegation of that paragraph.

45. The Defendants admit that claim 1 of the '172 Patent recites:

> A method for amplifying and sequencing DNA, comprising:
>
> isolating cell-free DNA from a biological sample and tagging the isolated cell- free DNA, wherein each tagged DNA molecule comprises a molecular barcode;
>
> performing a first PCR to simultaneously amplify at least 10 target loci using a universal primer and at least 10 target-specific primers in a single reaction volume;
>
> performing a second, nested PCR to simultaneously amplify the at least 10 target loci using the universal primer and at least 10 inner target-specific primers in a single reaction volume;
>
> performing high-throughput sequencing to sequence the amplified DNA comprising the target loci.

The Defendants admit that claim 1 recites a "method for amplifying and sequencing DNA" and further recites "PCR" and "high-throughput sequencing." Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 45 of the Second Amended Complaint.

46. The Defendants admit that a document purporting to be a copy of the '482 Patent is attached to the Second Amended Complaint as Exhibit 3. The Defendants admit that, on its face, the '482 Patent, titled "Amplification of cell-free DNA using nested PCR," indicates that it was issued by the USPTO on March 17, 2020. As to the remaining allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations

of paragraph 46 of the Second Amended Complaint, and therefore deny each and every allegation of that paragraph.

47. The Defendants deny that the claim language recited in paragraph 47 of the Amended Complaint reflects claim 1 of the '482 Patent. The Defendants admit that claim 1 of the '482 Patent actually recites:

> A method for nested PCR amplification, comprising:
>
> isolating cell-free DNA from a biological sample and ligating adaptors to the isolated cell-free DNA, wherein the adaptors each comprise a universal priming site;
>
> performing a first PCR to simultaneously amplify at least 10 target loci using a universal primer and at least 10 target-specific primers in a first reaction volume; and
>
> performing a second, nested PCR to simultaneously amplify the at least 10 target loci using the universal primer and at least 10 inner target-specific primers in a second reaction volume to obtain amplified DNA, wherein primer binding sites of the inner target-specific primers of the second PCR are internal to primer binding sites of the target-specific primers of the first PCR, wherein at least 80% of the amplified DNA maps to the target loci.

The Defendants admit that claim 1 recites a "method for nested PCR amplification" and further recites "a first reaction volume" and "a second reaction volume." Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 47 of the Second Amended Complaint.

48. The Defendants admit that a document purporting to be a copy of the '708 Patent is attached to the Second Amended Complaint as Exhibit 4. The Defendants admit that, on its face, the '708 Patent, titled "Methods for Simultaneous Amplifications of Target Loci," indicates that it was issued by the USPTO on March 24, 2020. As to the remaining allegations, the Defendants is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 48 of the Second Amended Complaint, and therefore deny each and every allegation of that paragraph.

49. The Defendants admit that claim 1 of the '708 Patent recites:

> A method for amplifying target loci in a nucleic acid sample, comprising:
>
> contacting the nucleic acid sample comprising target loci with a library of at least 2 primers that simultaneously hybridize to at least 2 of the target loci to produce a reaction mixture;
>
> subjecting the reaction mixture to primer extension reaction conditions to produce amplified products comprising target amplicons; wherein the annealing temperature for the reaction conditions is greater than a melting temperature of the at least 2 primers, wherein the length of the annealing step of the reaction conditions is greater than 3 minutes, and wherein the at least 2 of the target loci are simultaneously amplified; and
>
> sequencing the amplified products.

The Defendants admit that claim 1 recites "a method for amplifying target loci in a nucleic acid sample" and further recites "a reaction mixture" and "reaction conditions." Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 49 of the Second Amended Complaint.

50. The Defendants admit that a document purporting to be a copy of the '220 Patent is attached to the *Natera, Inc. v. ArcherDX, Inc.*, Case No. 20-cv-1047 (D. Del.), Complaint as Exhibit 5. The Defendants admit that, on its face, the '220 Patent, titled "Methods for Simultaneous Amplification of Target Loci," indicates that it was issued by the USPTO on August 4, 2020. As to the remaining allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 50 of the Second Amended Complaint, and therefore deny each and every allegation in that paragraph.

51. The Defendants admit that Natera, Inc. is listed as the assignee on the face of the '220 Patent. The Defendants deny that the '220 Patent is valid and enforceable. The Defendants aver that the '220 Patent is invalid for failure to satisfy one or more conditions for patentability set forth under 35 U.S.C. including but not limited to §§ 101, 102, 103, and 112 et seq.; no one associated with Natera invented the claimed methods; and the '220 Patent is unenforceable against

the Defendants by reason of Natera's inequitable conduct, unclean hands, and prosecution laches. As to the remaining allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 51 of the Second Amended Complaint, and therefore deny each and every allegation in that paragraph.

52. The Defendants admit that, on its face, the '220 Patent states that it issued from Application No. 16/743,724 and lists a filing date of January 15, 2020. The Defendants admit that, on its face, the '220 Patent states that it is a continuation of Application No. 16/399,268, which is a continuation of Application 16/140,298, which is a continuation of Application No. 14/918,544 filed on October 20, 2015. As to the remaining allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 52 of the Second Amended Complaint, and therefore deny each and every allegation in that paragraph.

53. The Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 53 of the Second Amended Complaint, and therefore deny each and every allegation in that paragraph.

54. The Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 54 of the Second Amended Complaint, and therefore deny each and every allegation in that paragraph.

55. The Defendants admit that claim 1 of the '220 Patent recites:

> A method for amplifying and sequencing DNA, comprising:
>
> ligating adaptors to cell-free DNA isolated from a biological sample, wherein the adaptors each comprises a universal priming sequence and a molecular barcode; performing a first PCR to simultaneously amplify at least 10 target loci using a universal primer and at least 10 target-specific primers in a single reaction volume; performing a second, nested PCR to simultaneously amplify the at least 10 target loci using a second universal primer and at least 10

> inner target-specific primers in a single reaction volume, wherein at least one of the primers comprises a sequencing tag; performing high-throughput sequencing to sequence the amplified DNA comprising the target loci.

The Defendants admit that claim 1 nominally recites a "method for amplifying and sequencing DNA" and further nominally recites "PCR" and "high-throughput sequencing." Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 55 of the Second Amended Complaint.

56. Paragraph 56 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in that paragraph. Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 35 of the Second Amended Complaint. The Defendants expressly deny that "the claims of the '814 patent cover methods of preparation," and further deny that such claims are analogous to claims that "were held not [to] be directed to a natural law or phenomenon in the recent Federal Circuit decision in *Illumina, Inc. v. Ariosa Diagnostics, Inc.*," 952 F.3d 1367 (Fed. Cir. 2020).

57. Paragraph 57 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in that paragraph. Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 57 of the Second Amended Complaint.

58. The Defendants admit the language appearing in the block quote in paragraph 58 of the Second Amended Complaint reflects a statement made by the USPTO examiner during the prosecution of the '814 Patent. The Defendants deny the allegation that "the USPTO examiner

found the claims to be non-routine and non-conventional." Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 58. Moreover, the Defendants aver that, contrary to the USPTO examiner's statement, "amplification of . . . circulating nucleic acids" is disclosed in the prior art, including in U.S. Patent App. Pub. No. 2010/0120038 ("Mir"). The Defendants further aver that "sequencing steps, . . . incorporat[ing] a universal or common primer, and . . . a sequencing tag" are also disclosed in the prior art, including in Mir. Natera disclosed Mir as one of *thousands* of references disclosed during prosecution of the '814 Patent.

59. The Defendants deny each and every allegation of paragraph 59 of the Second Amended Complaint.

60. Paragraph 60 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in that paragraph. Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 60 of the Second Amended Complaint. The Defendants expressly deny that "the claims of the '172 patent cover methods of preparation," and further deny that such claims are analogous to claims that "were held not [to] be directed to a natural law or phenomenon in the recent Federal Circuit decision in *Illumina, Inc. v. Ariosa Diagnostics, Inc.*," 952 F.3d 1367 (Fed. Cir. 2020).

61. Paragraph 61 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in that paragraph. Indeed, as set forth in the

Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 61 of the Second Amended Complaint.

62. The Defendants admit the language appearing in the block quote in paragraph 62 of the Second Amended Complaint reflects a statement made by the USPTO examiner during the prosecution of the '172 Patent. The Defendants deny the allegation that "the USPTO examiner found the claims to be non-routine and non-conventional." Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 62. Moreover, the Defendants aver that, contrary to the USPTO examiner's statement, "amplification of . . . circulating nucleic acids" is disclosed in the prior art, including in Mir. The Defendants further aver that "sequencing steps, . . . incorporat[ing] a universal or otherwise common primer" are also disclosed in the prior art, including in Mir. Natera disclosed Mir as one of *thousands* of references disclosed during prosecution of the '172 Patent.

63. Paragraph 63 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in that paragraph. Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 63 of the Second Amended Complaint. The Defendants expressly deny that "the claims of the '482 patent cover methods of preparation," and further deny that such claims are analogous to claims that "were held not [to] be directed to a natural law or phenomenon in the recent Federal Circuit decision in *Illumina, Inc. v. Ariosa Diagnostics, Inc.*," 952 F.3d 1367 (Fed. Cir. 2020).

64. Paragraph 64 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in that paragraph. Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 64 of the Second Amended Complaint.

65. The Defendants admit the language appearing in the block quote in paragraph 65 of the Second Amended Complaint reflects a statement made by the USPTO examiner during the prosecution of the '482 Patent. The Defendants deny the allegation that "the USPTO examiner found the claims to be non-routine and non-conventional." Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 65. Moreover, the Defendants aver that, contrary to the USPTO examiner's statement, "'nested PCR' following the recited 'first PCR' of 'cell-free DNA'" is disclosed in the prior art, including in Mir. Natera disclosed Mir as one of *thousands* of references disclosed during prosecution of the '482 Patent.

66. Paragraph 66 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in that paragraph. Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 66 of the Second Amended Complaint. The Defendants expressly deny that "the claims of the '708 patent cover methods of preparation," and further deny that such claims are analogous to claims that "were held not [to] be directed to a natural law or phenomenon in the recent Federal Circuit decision in *Illumina, Inc. v. Ariosa Diagnostics, Inc.*," 952 F.3d 1367 (Fed. Cir. 2020).

67. Paragraph 67 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in that paragraph. Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 67 of the Second Amended Complaint.

68. The Defendants admit the language appearing in the block quote in paragraph 68 of the Second Amended Complaint reflects a statement made by the USPTO examiner during the prosecution of the '708 Patent. The Defendants deny the allegation that "the USPTO examiner found the claims to be non-routine and non-conventional." Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 68. Moreover, the Defendants aver that, contrary to the USPTO examiner's statement, "the selection of an annealing temperature higher than the melting temperature of the primers, the selection of a long annealing time and sequencing of the amplification products" is disclosed in the prior art, including in International App. No. WO 2013/169339 ("Iafrate") and U.S. Patent App. Pub. No. 2012/270212 ("Rabinowitz"). Natera disclosed a related Iafrate application (U.S. Patent App. Pub. No. 2013/0303461) and Rabinowitz as two of *thousands* of references disclosed during prosecution of the '708 Patent.

69. Paragraph 69 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in paragraph 69 of the Complaint. Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 69 of the Complaint. The Defendants expressly denies that "[t]he claims are directed to an improved process of preparing non-natural

DNA," and further deny that such claims are analogous to claims that were "found patentable in *Illumina, Inc. v. Ariosa Diagnostics, Inc.*, 967 F.3d 1319 (Fed. Cir. Aug. 3, 2020)."

70. Paragraph 70 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent paragraph 70 excerpts the '220 Patent, the document speaks for itself. Except as expressly admitted herein, to the extent a response is required, the Defendants deny each and every allegation in paragraph 70 of the Second Amended Complaint.

71. Paragraph 71 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in that paragraph. Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 71 of the Second Amended Complaint.

72. Paragraph 72 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in that paragraph. Indeed, as set forth in the Defendants' Counterclaims, Natera's own admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 72 of the Second Amended Complaint.

73. The Defendants admit the language appearing in the block quote in paragraph 73 of the Second Amended Complaint reflects a statement made by the USPTO examiner during the prosecution of the '220 Patent. To the extent a response is required, the Defendants deny each and every allegation in paragraph 73 of the Second Amended Complaint. The Defendants specifically deny the allegation that "the USPTO examiner found the claims to be non-routine and non-conventional." Indeed, as set forth in the Defendants' Counterclaims, Natera's own

admissions made in court filings in this District and elsewhere contradict the allegations of paragraph 73. Moreover, the Defendants aver that, contrary to the USPTO examiner's statement, "multiplex using universal or common primers, and a second step of nested amplification" is disclosed in the prior art, including in U.S. Patent App. Pub. No. 2010/0120038 ("Mir"). Natera disclosed Mir as one of thousands of references during prosecution of the '220 Patent.

74. Paragraph 74 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in paragraph 74 of the Second Amended Complaint.

ARCHERDX'S ALLEGED INFRINGING ACTIVITIES

75. The Defendants deny that it and/or its end-users "perform every step of claim 1 of the Asserted Patents when they use any of the Accused Products." To the extent that paragraph 75 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 75 of the Second Amended Complaint.

76. The Defendants admit that ArcherDX, Inc. operates a CLIA-certified laboratory. The Defendants deny that they perform "every step of claim 1 of the Asserted Patents when using the Accused Products in the laboratory and sequencing the amplified DNA." Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 76 of the Second Amended Complaint.

77. Paragraph 77 of the Second Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every allegation in paragraph 77 of the Second Amended Complaint.

78. The Defendants aver that ArcherDX, Inc.'s Amended Complaint in *ArcherDX, Inc. v. Qiagen Sciences, LLC*, Case No. 18-1019 MN (D. Del.), D.I. 130, ¶ 20, states, "The

VariantPlex® , FusionPlex® , Reveal ctDNA™, and Immunoverse™ products, including custom kits, are sold as 'research use only' products to customers, including researchers clinical laboratories, contract research organizations, and pharmaceutical and biotechnology companies (collectively, 'End- users')." Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 78 of the Second Amended Complaint.

79. The Defendants admit that the quoted language appears in ArcherDX, Inc.'s Amended Complaint in *ArcherDX, Inc. v. Qiagen Sciences, LLC*, Case No. 18-1019 MN (D. Del.), D.I. 130, ¶ 20. The Defendants aver that the paragraph refers to the specific products VariantPlex® , FusionPlex® , Reveal ctDNA™, and Immunoverse™, and states, "Archer sells various products within four product lines that utilize AMP technology: VariantPlex® , FusionPlex® , Reveal ctDNA™, and Immunoverse™." Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 79 of the Second Amended Complaint.

80. The Defendants admit that a document purporting to be a claim chart for the Asserted Patents, and documents cited in the claim chart, are attached to the Second Amended Complaint as Exhibits 6-10 and Exhibits 12-41, respectively. The claim chart contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants specifically deny each and every allegation in the claim chart, and further deny that Exhibits 12-41 support the allegations, opinions, and legal conclusions in the claim chart. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 80 of the Second Amended Complaint.

81. Exhibits 6-10 contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, the Defendants deny each and every

allegation in Exhibits 6-10. The Defendants further deny each and every allegation in paragraph 81 of the Second Amended Complaint.

82. The allegations of paragraph 82 of the Second Amended Complaint constitute legal conclusions that require no response. The Defendants admit that LIQUIDPlex™ and VariantPlex® are products sold for research use only and use ArcherDX's proprietary AMP™ chemistry. The Defendants further admits that ArcherDX is currently developing its STRATAFIDE™ and PCM products for approval or clearance by the FDA as IVDs. The Defendants further admit that Archer®MET is an IVD product that has been approved in Japan only. The Defendants admit that AMP™ stands for "Anchored Multiplex PCR." The Defendants admit that ArcherDX's technology is utilized to preferentially enrich highly fragmented ctDNA, DNA, or RNA. Except as expressly admitted herein, to the extent a response is required, the Defendants deny each and every allegation in paragraph 82 of the Second Amended Complaint.

83. The allegations of paragraph 83 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 83 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is required, the Defendants deny each and every allegation in paragraph 83 of the Second Amended Complaint.

84. To the extent that paragraph 84 excerpts the contents of a journal article, the document speaks for itself. The Defendants admit that the product formerly called Reveal ctDNA™ is now called LiquidPlex™. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 84 of the Second Amended Complaint.

85. The allegations of paragraph 85 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 85 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 85 of the Second Amended Complaint.

86. The allegations of paragraph 86 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 86 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 86 of the Second Amended Complaint.

87. The allegations of paragraph 87 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 87 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 87 of the Second Amended Complaint.

88. To the extent that paragraph 88 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 88 of the Second Amended Complaint.

89. The allegations of paragraph 89 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 89 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 89 of the Second Amended Complaint.

90. The allegations of paragraph 90 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 90 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 90 of the Second Amended Complaint.

91. The allegations of paragraph 91 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 91 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 91 of the Second Amended Complaint.

92. To the extent that paragraph 92 excerpts the contents of a journal article, the document speaks for itself. The Defendants are without knowledge or information sufficient to form a belief as to the truth of the remaining allegations, and therefore deny each and every remaining allegation in paragraph 92 of the Second Amended Complaint.

93. To the extent that paragraph 93 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 93 of the Second Amended Complaint.

94. The Defendants deny each and every allegation in paragraph 94 of the Second Amended Complaint.

95. To the extent that paragraph 95 excerpts the contents of a journal article, the document speaks for itself. To the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 95 of the Second Amended Complaint.

96. The allegations of paragraph 96 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 96 of the Second Amended Complaint.

97. The allegations of paragraph 97 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 97 of the Second Amended Complaint.

98. The Defendants admit that the LIQUIDPlex™ technology uses AMP™ chemistry to create target-enriched libraries for next-generation sequencing (NGS). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 98 of the Second Amended Complaint.

99. To the extent that paragraph 99 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 99 of the Second Amended Complaint.

100. To the extent that paragraph 100 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 100 of the Second Amended Complaint.

101. The Defendants admit that the VariantPlex technology uses AMP™ chemistry to create target-enriched libraries for next-generation sequencing (NGS). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 101 of the Second Amended Complaint.

102. To the extent that paragraph 102 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 102 of the Second Amended Complaint.

103. To the extent that paragraph 103 excerpts the contents of an ArcherDX document, the document speaks for itself. The Defendants admit that PCM is intended to be a bespoke product—adjusted as needed on a patient-by-patient basis. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 103 of the Second Amended Complaint.

104. The allegations of paragraph 104 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 104 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 104 of the Second Amended Complaint.

105. To the extent that paragraph 105 excerpts the contents of a journal article, the document speaks for itself. The Defendants are without knowledge or information sufficient to form a belief as to the truth of the remaining allegations, and therefore deny each and every remaining allegation in paragraph 105 of the Second Amended Complaint.

106. To the extent that paragraph 106 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted, the Defendants deny each and every allegation in paragraph 106 of the Second Amended Complaint.

107. To the extent that paragraph 107 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 107 of the Second Amended Complaint.

108. The Defendants deny each and every allegation in paragraph 108 of the Second Amended Complaint.

109. To the extent that paragraph 109 excerpts the contents of a journal article, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 109 of the Second Amended Complaint.

110. The allegations of paragraph 110 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 110 of the Second Amended Complaint.

111. The allegations of paragraph 111 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 111 of the Second Amended Complaint.

112. The allegations of paragraph 112 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 112 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 112 of the Second Amended Complaint.

113. The allegations of paragraph 113 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 113 of the Second Amended Complaint.

114. To the extent that paragraph 114 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as express admitted herein, the Defendants deny each and every allegation in paragraph 114 of the Second Amended Complaint.

115. To the extent that paragraph 115 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 115 of the Second Amended Complaint.

116. The allegations of paragraph 116 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 116 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 116 of the Second Amended Complaint.

117. The allegations of paragraph 117 of the Second Amended Complaint constitute legal conclusions that require no response. Except as expressly admitted herein, to the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 117 of the Second Amended Complaint.

118. ArcherDX admits that LIQUIDPlex™ utilizes ArcherDX's proprietary AMP™ technology. To the extent that paragraph 83 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 118 of the Second Amended Complaint.

119. The Defendants admit that LIQUIDPlex™ and VariantPlex® utilize ArcherDX's proprietary AMP™ technology and have application for solid tumors as well as hematological malignancies. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 119 of the Second Amended Complaint.

120. The Defendants admit that VariantPlex® utilizes ArcherDX's proprietary AMP™ technology. To the extent that paragraph 120 excerpts the contents of an ArcherDX document,

the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 120 of the Second Amended Complaint.

121. The Defendants admit that VariantPlex® utilizes ArcherDX's proprietary AMP™ technology. To the extent that paragraph 121 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 121 of the Second Amended Complaint.

122. The Defendants admit that LIQUIDPlex™ and VariantPlex® are products available for research use only and are not IVDs. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 122 of the Second Amended Complaint.

123. The allegations of paragraph 123 of the Second Amended Complaint constitute legal conclusions that require no response. The Defendants admit that LIQUIDPlex™ is a product available for research use only and is not an IVD. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 123 of the Second Amended Complaint.

124. The allegations of paragraph 124 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants specifically deny that they have or have had the requisite intent or knowledge to induce or contribute to the direct infringement of the Asserted Patent by another. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 124 of the Second Amended Complaint.

125. The allegations of paragraph 125 of the Complaint constitute legal conclusions that require no response. The Defendants admit that VariantPlex® is a product available for research

use only and is not an IVD. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 125 of the Second Amended Complaint.

126. The allegations of paragraph 126 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants specifically deny that they have or have had the requisite intent or knowledge to induce or contribute to the direct infringement of the Asserted Patent by another. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 126 of the Second Amended Complaint.

127. The Defendants admit that Archer®MET utilizes ArcherDX's proprietary AMP™ technology. To the extent that paragraph 127 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 127 of the Second Amended Complaint.

128. The Defendants admit that Archer®MET has been recently approved in Japan only. Natera's allegations fail to state a claim upon which relief may be granted. For example, paragraph 128 of the Complaint does not plausibly allege that the Defendants have engaged in any activities with respect to Archer®MET that would constitute patent infringement under 35 U.S.C. § 271. The Asserted Patent recites only method claims, which cannot, as a matter of law, be infringed by the alleged manufacturing of the Archer®MET product in the United States or the alleged exporting of the Archer®MET product from the United States. Indeed, the alleged shipment of the Archer®MET product overseas cannot constitute infringement "as Section 271(f) does not encompass devices that may be used to practice a patented method." *Cardiac Pacemakers, Inc. v. St. Jude Medical, Inc.*, 576 F.3d 1348, 1365 (Fed. Cir. 2009) (en banc).

Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 128 of the Second Amended Complaint.

129. To the extent that paragraph 129 excerpts the contents of an ArcherDX document, the document speaks for itself. Natera's allegations fail to state a claim upon which relief may be granted. For example, paragraph 129 of the Second Amended Complaint does not plausibly allege that the Defendants have engaged in any activities with respect to Archer®MET that would constitute patent infringement under 35 U.S.C. § 271. The Asserted Patent recites only method claims, which cannot, as a matter of law, be infringed by the alleged manufacturing of the Archer®MET product in the United States or the alleged exporting of the Archer®MET product from the United States. Indeed, the alleged shipment of the Archer®MET product overseas cannot constitute infringement "as Section 271(f) does not encompass devices that may be used to practice a patented method." *Cardiac Pacemakers, Inc. v. St. Jude Medical, Inc.*, 576 F.3d 1348, 1365 (Fed. Cir. 2009) (en banc). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 129 of the Second Amended Complaint.

130. To the extent that paragraph 130 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 130 of the Second Amended Complaint.

131. The allegations of paragraph 131 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants specifically deny that they performed in the United States any claimed method of the Asserted Patents. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 131 of the Second Amended Complaint.

132. The Defendants aver that ArcherDX is currently developing its STRATAFIDE™ IVD product for approval or clearance by the FDA. To the extent that paragraph 132 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 132 of the Second Amended Complaint.

133. The Defendants aver that ArcherDX is currently developing its PCM IVD product for approval or clearance by the FDA. The Defendants aver that PCM is intended to be a bespoke product— adjusted as needed on a patient-by-patient basis. To the extent paragraph 133 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 133 of the Second Amended Complaint.

134. To the extent paragraph 134 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 134 of the Second Amended Complaint.

135. To the extent paragraph 135 excerpts the contents of ArcherDX documents, those documents speak for themselves. The Defendants aver that STRATAFIDE and PCM are in development as IVDs. As FDA guidance explains, one type of RUO "is an IVD product that is in the laboratory research phase of development." *Natera, Inc. v. ArcherDX, Inc.*, Case No. 20-cv-1047-LPS (D. Del.), D.I. 1, Ex. 21 at 7. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 135 of the Second Amended Complaint. Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of

a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Archercannot commercialize any IVD product without first obtaining FDA approval. Indeed, Natera fails to allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1).

136. The allegations of paragraph 136 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants deny each and every allegation in paragraph 136 of the Second Amended Complaint. The Defendants specifically deny that they have engaged in activities with respect to STRATAFIDE and PCM not reasonably related to FDA approval. Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Archer cannot commercialize any IVD product without first obtaining FDA approval. Indeed, Natera fails to allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1).

137. The Defendants deny each and every allegation in paragraph 137 of the Second Amended Complaint. As FDA guidance explains, one type of RUO "is an IVD product that is in the laboratory research phase of development." *Natera, Inc. v. ArcherDX, Inc.*, Case No. 20-cv-1047-LPS (D. Del.), D.I. 1, Ex. 21 at 7. Uses of products in development as IVDs that require FDA approval are within 35 U.S.C. 271(e)(1)'s safe harbor. *See Eli Lilly & Co v. Medtronic,*

Inc., 496 U.S. 661 (1990). Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. The Defendants cannot commercialize any IVD product without first obtaining FDA approval. Indeed, Natera fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1).

138. The allegations of paragraph 138 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 138 refers to the contents of an ArcherDX document, the document speaks for itself. The Defendants aver that the TRACERx investigators, led by Professor Charles Swanton, Group Leader, University College London ("UCL") and the Francis Crick Institute, and Dr. Christopher Abbosh, Principal Clinical Fellow, UCL, are utilizing ArcherDX's technology—and not Natera's inferior technology—to detect low-volume minimal residual disease at high levels of sensitivity to help achieve TRACERx's goal of a more personalized approach to developing cancer treatments. Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. The Defendants cannot commercialize any IVD product without first obtaining FDA approval.

Indeed, Natera fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 138 of the Second Amended Complaint.

139. The allegations of paragraph 139 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 139 refers to the contents of an ArcherDX document, the document speaks for itself. Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Archer cannot commercialize any IVD product without first obtaining FDA approval. Indeed, Natera fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 139 of the Second Amended Complaint.

140. The allegations of paragraph 140 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 140 refers to the contents of an ArcherDX document, the document speaks for itself. The Defendants aver that Exhibit 17 to the Second Amended Complaint states that PCM is "currently an investigational device." Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim

of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Archer cannot commercialize any IVD product without first obtaining FDA approval. Indeed, Natera fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 140 of the Second Amended Complaint.

141. The allegations of paragraph 141 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent that paragraph 141 refers to the contents of an ArcherDX document, the document speaks for itself. The Defendants aver that Exhibit 26 to the Second Amended Complaint states, "The assays are currently for investigational use only." Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. ArcherDX cannot commercialize any IVD product without first obtaining FDA approval. Indeed, Natera fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 141 of the Second Amended Complaint.

142. The allegations of paragraph 142 of the Second Amended Complaint constitute legal conclusions that require no response. Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Archer cannot commercialize any IVD product without first obtaining FDA approval. Indeed, Natera fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). The Defendants deny each and every allegation in paragraph 142 of the Second Amended Complaint.

143. The allegations of paragraph 143 of the Second Amended Complaint constitute legal conclusions that require no response. Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Archer cannot commercialize any IVD product without first obtaining FDA approval. Indeed, Natera fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 143 of the Second Amended Complaint.

144. To the extent that paragraph 144 excerpts the contents of an ArcherDX document, the document speaks for itself. ArcherDX specifically denies that it "received [any] financing as a result of its infringing use of Natera's patented technology." Natera's allegation that ArcherDX "announced the close of a $55 million Series C financing round, the proceeds of which are intended to be used to support the launch of Stratafide and PCM" (emphasis added) fails to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. The Defendants cannot commercialize any IVD product without first obtaining FDA approval. Moreover, Natera also fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 144 of the Second Amended Complaint.

145. To the extent that paragraph 145 excerpts the contents of an ArcherDX document, the document speaks for itself. The Defendants specifically deny that they "ha[ve] commercially benefited and will benefit from the infringing use of PCM and STRATAFIDE by others." Natera fails to allege how the alleged licensing activities constitute a commercial sale or offer for sale. Natera's allegations that ArcherDX "anticipated that Stratafide ***would be the first IVD*** to be marketed under the partnership between [ArcherDX] and Illumina" and that ArcherDX "announced that it ***planned to launch PCM for diagnostic use*** as part of this commercial partnership" (emphasis added) fail to give rise to a case or controversy between the parties under

Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. The Defendants cannot commercialize any IVD product without first obtaining FDA approval. Indeed, Natera fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 145 of the Second Amended Complaint.

146. The Defendants aver that the TRACERx investigators, led by Professor Charles Swanton, Group Leader, University College London ("UCL") and the Francis Crick Institute, and Dr. Christopher Abbosh, Principal Clinical Fellow, UCL, are utilizing ArcherDX's technology—and not Natera's inferior technology—to detect low-volume minimal residual disease at high levels of sensitivity to help achieve TRACERx's goal of a more personalized approach to developing cancer treatments. Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. The Defendants cannot commercialize any IVD product without first obtaining FDA approval. Indeed, Natera fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Natera's allegations further fail to state a claim upon

which relief may be granted. Paragraph 146 of the Second Amended Complaint does not plausibly allege that the Defendants have engaged in any activities with respect to the TRACERx study that would constitute patent infringement under 35 U.S.C. § 271. The Asserted Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting those components (e.g., kits) from the United States. Exporting components (e.g., kits) overseas cannot constitute infringement of method claims "as Section 271(f) does not encompass devices that may be used to practice a patented method." *Cardiac Pacemakers, Inc. v. St. Jude Medical, Inc.*, 576 F.3d 1348, 1365 (Fed. Cir. 2009) (en banc). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 146 of the Second Amended Complaint.

147. The Defendants admit that ArcherDX received the FDA's Breakthrough Device Designation for STRATAFIDE™ in December 2018. Natera's allegation that ArcherDX "intends to sell the product for diagnostic use immediately upon approval" (emphasis added) fails to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. The Defendants cannot commercialize any IVD product without first obtaining FDA approval. Paragraph 147 of the Second Amended Complaint further fails to plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 147 of the Second Amended Complaint.

148. The Defendants admit that ArcherDX received the FDA's Breakthrough Device Designation for PCM in January 2020. Natera's allegation that ArcherDX "intends to sell the product for diagnostic use immediately upon approval" (emphasis added) fails to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. The Defendants cannot commercialize any IVD product without first obtaining FDA approval. Paragraph 148 of the Second Amended Complaint further fails to plausibly allege that the Defendants have engaged in any activities with respect to PCM that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 148 of the Second Amended Complaint.

149. The allegations of paragraph 149 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants specifically deny that they have or have had the requisite intent or knowledge to induce or contribute to the direct infringement of the Asserted Patent by another. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 149 of the Second Amended Complaint.

150. The allegations of paragraph 150 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants specifically deny that they have or have had the requisite intent or knowledge to induce or contribute to the direct infringement of the Asserted Patent by another. Except as expressly

admitted herein, the Defendants deny each and every allegation in paragraph 150 of the Second Amended Complaint.

151. The Defendants deny each and every allegation in paragraph 151 of the Second Amended Complaint. ArcherDX avers that it developed its own proprietary AMP™ chemistry, technology platform, and applications.

152. To the extent that paragraph 152 excerpts the contents of an ArcherDX document, the document speaks for itself. The Defendants aver that the TRACERx investigators, led by Professor Charles Swanton, Group Leader, UCL and the Francis Crick Institute, and Dr. Christopher Abbosh, Principal Clinical Fellow, UCL, are utilizing ArcherDX's technology—and not Natera's inferior technology—to detect low-volume minimal residual disease at high levels of sensitivity to help achieve TRACERx's goal of a more personalized approach to developing cancer treatments. Paragraph 152 of the Second Amended Complaint further contains legal conclusions that require no response. To the extent paragraph 152 contains factual allegations, the Defendants are without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore deny each and every allegation in that paragraph.

153. The Defendants deny each and every allegation in paragraph 153 of the Second Amended Complaint. ArcherDX avers that it developed its own proprietary AMP™ chemistry, technology platform, and applications.

154. The Defendants admit that LIQUIDPlex™, VariantPlex®, and FusionPlex® utilize ArcherDX's proprietary AMP™ technology to preferentially enrich highly fragmented ctDNA, DNA, or RNA and have application for solid tumors as well as hematological malignancies. LIQUIDPlex™, VariantPlex®, and FusionPlex® are products available for research use only (as

opposed to IVDs). Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 154 of the Second Amended Complaint.

155. The Defendants admit that FusionPlex® is a product available for research use only, and not for the diagnosis or treatment of disease; FusionPlex® is not an IVD. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 155 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '482 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product that is used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a

claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

156. The allegations of paragraph 156 of the Second Amended Complaint constitute legal conclusions that require no response. To the extent a response is deemed required, the Defendants specifically deny that they have or have had the requisite intent or knowledge to induce or contribute to the direct infringement of any Asserted Patent by another. The Defendants deny each and every other allegation of paragraph 156 of the Second Amended Complaint.

157. To the extent that paragraph 157 recites an ArcherDX document, the document speaks for itself. The Defendants are without knowledge or information sufficient to form a belief as to how Natera monetizes its technology and, on that basis, deny that Natera is a "direct competitor." Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 157 of the Second Amended Complaint.

158. Archer admits that it gained knowledge of the '814 Patent after it received a copy of the initial complaint in this action. Invitae admits that it gained knowledge of the '814 Patent at least as early of the date of the Second Amended Complaint. Except as expressly admitted herein, the Defendants denies each and every allegation of paragraph 158 of the Second Amended Complaint.

159. Archer has knowledge of the '172 patent at least as early as the date of this first amended complaint in this action. Invitae admits that it gained knowledge of the '172 Patent at least as early of the date of the Second Amended Complaint.

160. Archer has knowledge of the '482 patent at least as early as the date of this first amended complaint in this action. Invitae admits that it gained knowledge of the '482 Patent at least as early of the date of the Second Amended Complaint.

161. Archer has knowledge of the '708 patent at least as early as the date of this first amended complaint in this action. Invitae admits that it gained knowledge of the '708 Patent at least as early of the date of the Second Amended Complaint.

162. Archer has knowledge of the '220 patent at least as early as the date of the complaint in *Natera, Inc. v. ArcherDX, Inc.*, Case No. 20-cv-1047-LPS (D. Del.). Invitae admits that it gained knowledge of the '220 Patent at least as early of the date of the Second Amended Complaint.

163. The Defendants admit to knowledge of the Asserted Patents at least as early as the dates set forth in ¶¶ 158-62. The Defendants specifically deny the alleged infringing activities. To the extent paragraph 163 contains factual allegations, Defendants neither admit nor deny the substance of those allegations and assert the attorney-client privilege and work product protections.

RESPONSE TO COUNT I: ALLEGED INFRINGEMENT OF THE '814 PATENT

164. The Defendants restate and incorporate by reference, their preliminary statement, and each and every response set forth above in paragraphs 1-163 of its Answer, as if fully set forth herein.

165. The Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 165 of the Second Amended Complaint, and therefore deny each and every allegation in that paragraph.

166. The Defendants deny each and every allegation of paragraph 166 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1).

Moreover, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '814 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

167. The Defendants deny each and every allegation of paragraph 167 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other

oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '814 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

168. The Defendants deny each and every allegation of paragraph 168 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '814 Patent

recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

169. The Defendants deny each and every allegation of paragraph 169 of the Second Amended Complaint.

170. The Defendants deny each and every allegation of paragraph 170 of the Second Amended Complaint.

RESPONSE TO COUNT II: REQUEST FOR DECLARATORY JUDGMENT RELATING TO ALLEGED FUTURE INFRINGEMENT OF THE '814 PATENT

171. The Defendants restate and incorporate by reference, its preliminary statement, and each and every response set forth above in paragraphs 1-170 of its Answer, as if fully set forth herein.

172. The Defendants admit that ArcherDX has received the FDA's Breakthrough Device Designation for STRATAFIDE™ and PCM. The Defendants deny that they have sought or received, or presently intends to seek, Breakthrough Device Designation for LIQUIDPlex™ from the FDA. Natera's allegation that ArcherDX "intends to engage in the commercial manufacture, use, offer for sale, and sale of the Accused Products ***if*** and when it receives FDA approval to do so" (emphasis added) fails to give rise to a case or controversy between the parties under Article

III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 172 of the Second Amended Complaint.

173. The Second Amended Complaint fails to plead facts supporting "[a]n actual, substantial, and justiciable controversy" with respect to at least STRATAFIDE™, PCM, and Archer®MET (and any other oncology products in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 173 of the Second Amended Complaint.

174. The Defendants deny each and every allegation of paragraph 174 of the Second Amended Complaint.

175. The Defendants deny each and every allegation of paragraph 175 of the Second Amended Complaint.

176. The Defendants deny each and every allegation of paragraph 176 of the Second Amended Complaint.

RESPONSE TO COUNT III: ALLEGED INFRINGEMENT OF THE '172 PATENT

177. The Defendants restate and incorporate by reference, its preliminary statement, and each and every response set forth above in paragraphs 1-176 of its Answer, as if fully set forth herein.

178. The Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 178 of the Second Amended Complaint, and therefore deny each and every allegation in that paragraph.

179. The Defendants deny each and every allegation of paragraph 179 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '172 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). In particular,

Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

180. The Defendants deny each and every allegation of paragraph 180 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '172 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim

that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

181. The Defendants deny each and every allegation of paragraph 181 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '172 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

182. The Defendants deny each and every allegation of paragraph 182 of the Second Amended Complaint.

183. The Defendants deny each and every allegation of paragraph 183 of the Second Amended Complaint.

RESPONSE TO COUNT IV: REQUEST FOR DECLARATORY JUDGMENT RELATING TO ALLEGED FUTURE INFRINGEMENT OF THE '172 PATENT

184. The Defendants restate and incorporate by reference, its preliminary statement, and each and every response set forth above in paragraphs 1-183 of its Answer, as if fully set forth herein.

185. The Defendants admit that ArcherDX has received the FDA's Breakthrough Device Designation for STRATAFIDE™ and PCM. The Defendants deny that they have sought or received, or presently intends to seek, Breakthrough Device Designation for LIQUIDPlex™ from the FDA. Natera's allegation that ArcherDX "intends to engage in the commercial manufacture, use, offer for sale, and sale of the Accused Products if and when it receives FDA approval to do so" (emphasis added) fails to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 185 of the Second Amended Complaint.

186. The Second Amended Complaint fails to plead facts supporting "[a]n actual, substantial, and justiciable controversy" with respect to at least STRATAFIDE™, PCM, and Archer®MET (or any other oncology product in development or any other oncology product used

overseas, and that utilizes the same technology as any of the Accused Products). Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 186 of the Second Amended Complaint.

187. The Defendants deny each and every allegation of paragraph 187 of the Second Amended Complaint.

188. The Defendants deny each and every allegation of paragraph 188 of the Second Amended Complaint.

189. The Defendants deny each and every allegation of paragraph 189 of the Second Amended Complaint.

RESPONSE TO COUNT V: ALLEGED INFRINGEMENT OF THE '482 PATENT

190. The Defendants restate and incorporate by reference, its preliminary statement, and each and every response set forth above in paragraphs 1-189 of its Answer, as if fully set forth herein.

191. The Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 191 of the Second Amended Complaint, and therefore deny each and every allegation in that paragraph.

192. The Defendants deny each and every allegation of paragraph 192 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology

as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '482 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

193. The Defendants deny each and every allegation of paragraph 193 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA

approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '482 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

194. The Defendants deny each and every allegation of paragraph 194 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other

oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '482 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product that is used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

195. The Defendants deny each and every allegation of paragraph 195 of the Second Amended Complaint.

196. The Defendants deny each and every allegation of paragraph 196 of the Second Amended Complaint.

RESPONSE TO COUNT VI: REQUEST FOR DECLARATORY JUDGMENT RELATING TO ALLEGED FUTURE INFRINGEMENT OF THE '482 PATENT

197. The Defendants restate and incorporate by reference, its preliminary statement, and each and every response set forth above in paragraphs 1-196 of its Answer, as if fully set forth herein.

198. The Defendants admit that ArcherDX has received the FDA's Breakthrough Device Designation for STRATAFIDE™ and PCM. The Defendants deny that they have sought or received, or presently intends to seek, Breakthrough Device Designation for LIQUIDPlex™ from

the FDA. Natera's allegation that ArcherDX "intends to engage in the commercial manufacture, use, offer for sale, and sale of the Accused Products if and when it receives FDA approval to do so" fails to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 198 of the Second Amended Complaint.

199. The Second Amended Complaint fails to plead facts supporting "[a]n actual, substantial, and justiciable controversy" with respect to at least STRATAFIDE™, PCM, and Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 199 of the Second Amended Complaint.

200. The Defendants deny each and every allegation of paragraph 200 of the Second Amended Complaint.

201. The Defendants deny each and every allegation of paragraph 201 of the Second Amended Complaint.

202. The Defendants deny each and every allegation of paragraph 202 of the Second Amended Complaint.

RESPONSE TO COUNT VII: ALLEGED INFRINGEMENT OF THE '708 PATENT

203. The Defendants restate and incorporate by reference, its preliminary statement, and each and every response set forth above in paragraphs 1-202 of its Answer, as if fully set forth herein.

204. The Defendants are without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 204 of the Second Amended Complaint, and therefore deny each and every allegation in that paragraph.

205. The Defendants deny each and every allegation of paragraph 205 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '708 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or

Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

206. The Defendants deny each and every allegation of paragraph 206 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '708 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). In particular,

Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

207. The Defendants deny each and every allegation of paragraph 207 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '708 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a

claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

208. The Defendants deny each and every allegation of paragraph 208 of the Second Amended Complaint.

209. The Defendants deny each and every allegation of paragraph 209 of the Second Amended Complaint.

RESPONSE TO COUNT VIII: REQUEST FOR DECLARATORY JUDGMENT RELATING TO ALLEGED FUTURE INFRINGEMENT OF THE '708 PATENT

210. The Defendants restate and incorporate by reference, its preliminary statement, and each and every response set forth above in paragraphs 1-209 of its Answer, as if fully set forth herein.

211. The Defendants admit that they have received the FDA's Breakthrough Device Designation for STRATAFIDE™ and PCM. The Defendants deny that they have sought or received, or presently intends to seek, Breakthrough Device Designation for LIQUIDPlex™, FusionPlex®, or VariantPlex® from the FDA. Natera's allegation that ArcherDX "intends to engage in the commercial manufacture, use, offer for sale, and sale of the Accused Products if and when it receives FDA approval to do so" (emphasis added) fails to give rise to a case or controversy between the parties under Article III of the Constitution and the Declaratory Judgment Act. Indeed, The Defendants cannot commercialize any IVD product without first obtaining FDA approval. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 211 of the Second Amended Complaint.

212. The Second Amended Complaint fails to plead facts supporting "[a]n actual,

substantial, and justiciable controversy" with respect to at least STRATAFIDE™, PCM, and Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation of paragraph 212 of the Second Amended Complaint.

213. The Defendants deny each and every allegation of paragraph 213 of the Second Amended Complaint.

214. The Defendants deny each and every allegation of paragraph 214 of the Second Amended Complaint.

215. The Defendants deny each and every allegation of paragraph 215 of the Second Amended Complaint.

RESPONSE TO COUNT IX: ALLEGED INFRINGEMENT OF THE '220 PATENT

216. The Defendants restate and incorporate by reference, its preliminary statement, and each and every response set forth above in paragraphs 1-215 of its Answer, as if fully set forth herein.

217. The Defendants deny each and every allegation in paragraph 217 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes

the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). The Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not plausibly allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '220 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

218. The Defendants deny each and every allegation in paragraph 218 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). The Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not

plausibly allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '220 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

219. The Defendants deny each and every allegation in paragraph 219 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). The Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not plausibly allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology

as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '220 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

220. The Defendants deny each and every allegation in paragraph 220 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). The Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not plausibly allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '220 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (e.g., kits) in the United States or exporting components (e.g., kits)

from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer®MET (or any other oncology product in development or used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

221. The Defendants deny each and every allegation in paragraph 221 of the Second Amended Complaint.

222. The Defendants deny each and every allegation in paragraph 222 of the Second Amended Complaint.

RESPONSE TO COUNT X: REQUEST FOR DECLARATORY JUDGMENT RELATING TO ALLEGED FUTURE INFRINGEMENT OF THE '220 PATENT

223. The Defendants restate and incorporate by reference, its preliminary statement, and each and every response set forth above in paragraphs 1-222 of its Answer, as if fully set forth herein.

224. The Defendants deny each and every allegation in paragraph 224 of the Second Amended Complaint. In addition, the Second Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted. For example, the Second Amended Complaint does not plausibly allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). The Defendants cannot commercialize any IVD product without first obtaining FDA approval. As another example, the Second Amended Complaint does not

plausibly allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The '220 Patent recites only method claims, which cannot, as a matter of law, be infringed by manufacturing components (*e.g.*, kits) in the United States or exporting components (*e.g.*, kits) from the United States. In addition, Natera's allegations fail to give rise to a case or controversy between the parties under Article III of the Constitution with respect to STRATAFIDE™, PCM, or Archer ®MET (or any other oncology product in development or used overseas, and that utilizes the same technology as any of the Accused Products). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

225. The Defendants admit that they have received the FDA's Breakthrough Device Designation for STRATAFIDE™ and PCM. Natera's allegation that ArcherDX "intends to engage in the commercial manufacture, use, offer for sale, and sale of the Accused Products if and when it receives FDA approval to do so" (emphasis added) fails to give rise to a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act. In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 225 of the Second Amended Complaint.

226. To the extent that paragraph 226 excerpts the contents of an ArcherDX document, the document speaks for itself. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 226 of the Second Amended Complaint.

227. The Second Amended Complaint fails to plausibly allege facts supporting "[a]n actual, substantial, and justiciable controversy" with respect to at least STRATAFIDE™, PCM, and Archer®MET (and any other oncology products in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 227 of the Second Amended Complaint.

228. The Second Amended Complaint fails to plausibly allege facts supporting an "immediate" controversy with respect to at least STRATAFIDE™, PCM, and Archer®MET (and any other oncology products in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). To the extent that paragraph 228 excerpts the contents of an ArcherDX document, the document speaks for itself. Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 228 of the Second Amended Complaint.

229. To the extent that paragraph 229 excerpts the contents of an ArcherDX document, the document speaks for itself. Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 229 of the Second Amended Complaint.

230. To the extent that paragraph 230 excerpts the contents of an ArcherDX document, the document speaks for itself. Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 230 of the Second Amended Complaint.

231. The Second Amended Complaint fails to plausibly allege facts supporting a "real" controversy with respect to at least STRATAFIDE™, PCM, and Archer®MET (and any other oncology products in development or any other oncology product used overseas, and that utilizes the same technology as any of the Accused Products). Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all. Except as expressly admitted herein, the Defendants deny each and every allegation in paragraph 231 of the Seconded Amended Complaint.

232. The Defendants deny each and every allegation in paragraph 232 of the Second Amended Complaint.

233. The Defendants deny each and every allegation in paragraph 233 of the Second Amended Complaint.

234. The Defendants deny each and every allegation in paragraph 234 of the Second Amended Complaint.

RESPONSE TO NATERA'S PRAYER FOR RELIEF

235. The Defendants deny that Natera is entitled to any relief from the Defendants, including the relief Natera seeks in Paragraphs (1)–(6) of its Prayer for Relief. Natera's Prayer for Relief should be denied in its entirety and with prejudice, and Natera should be awarded nothing. The Defendants further deny each and every allegation in Natera's Prayer for Relief.

ARCHERDX'S DEFENSES

236. The Defendants allege and assert the following defenses in response to the allegations in the Second Amended Complaint, undertaking the burden of proof only as to those defenses deemed affirmative defenses by law, regardless of how such defenses are denominated herein. The Defendants reserve the right to amend its Answer, including to modify, amend, and/or expand upon its defenses once discovery progresses. Without conceding that any of the following defenses must necessarily be pled, or that any of the following defenses is not already at issue by virtue of the foregoing denials, and without reducing or removing Natera's burdens of proof on its affirmative claims against the Defendants, the Defendants allege and assert as follows:

FIRST DEFENSE
(Failure to State a Claim)

237. The allegations and claims in the Second Amended Complaint, in whole or in part, fail to state a claim upon which relief may be granted.

238. The Second Amended Complaint fails to plead any specific instances of infringement by the use of any Accused Products. It pleads only that Archer's AMP process "can" perform a claimed method step. *See*, *e.g.*, D.I. 17, ¶¶ 58-97. However, none of the claims of the Asserted Patents require merely the capacity to perform a certain step. Accordingly, the Second Amended Complaint fails to plead that any Accused Products was actually used in an infringing manner. *See Fujitsu Ltd. v. Netgear Inc.*, 620 F.3d 1321, 1329 (Fed. Cir. 2010).

239. The Second Amended Complaint also does not allege that the Defendants have engaged in any activities with respect to STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) that fall outside the safe harbor provided by 35 U.S.C. § 271(e)(1). Indeed, the Defendants cannot commercialize any IVD product without first obtaining FDA approval.

240. Furthermore, the Second Amended Complaint does not allege that the Defendants have engaged in any activities in the U.S. with respect to Archer®MET (or any other oncology product used overseas and that utilizes the same technology as any of the Accused Products) that would constitute patent infringement under 35 U.S.C. § 271. The Asserted Patents recite only method claims, which cannot, as a matter of law, be infringed by the alleged manufacturing of the Archer®MET product, or any other product, in the United States or the alleged exportation from the United States of the Archer®MET, or any other, product. Indeed, the alleged shipment of the Archer®MET product, or any other product, overseas cannot constitute infringement "as Section 271(f) does not encompass devices that may be used to practice a patented method." *Cardiac Pacemakers, Inc. v. St. Jude Medical, Inc.*, 576 F.3d 1348, 1365 (Fed. Cir. 2009) (en banc).

241. The Second Amended Complaint further fails to state a claim upon which relief may be granted because, as set forth in the Defendants' Counterclaims, the claims of the Asserted Patents are invalid under one or more of 35 U.S.C. § 101, 102, 103, 112, et seq.

SECOND DEFENSE
(Lack of Subject Matter Jurisdiction)

242. There is no subject matter jurisdiction because the Second Amended Complaint fails to plead a case or controversy between the parties under Article III of the Constitution or the Declaratory Judgment Act, 28 U.S.C. § 2201 et seq. with respect to ArcherDX's IVD products (including any oncology product in development or any oncology product used overseas). In particular, Natera fails to plead a claim of sufficient immediacy and reality to give rise to Article III jurisdiction or to warrant the issuance of a declaratory judgment. Natera also fails to plead a claim that is ripe for adjudication as it rests upon contingent or future events that may not occur as anticipated, or may not occur at all.

243. None of the Accused Products are presently cleared or approved by the FDA. The Defendants have not sought or received, nor does it presently intend to seek, Breakthrough Device Designation or premarket approval or approval or clearance pursuant to 21 U.S.C. § 360(k) ("510k approval or clearance") from the FDA for LIQUIDPlex™, FusionPlex®, VariantPlex®, or Archer®MET. Archer®MET has been approved, and is only sold in, Japan. LIQUIDPlex™, FusionPlex®, and VariantPlex® are sold in the U.S. as research use only (or "RUO") products, which in contrast to IVD products, do not require FDA approval prior to commercialization. Indeed, both STRATAFIDE™ and PCM, which are IVD products, require premarket approval or

510k approval or clearance to be sold commercially. The Defendants have not, however, even submitted an application for FDA clearance or approval to the FDA for either STRATAFIDE™ or PCM.

244. The development of the data necessary to obtain regulatory clearance and/or approval of STRATAFIDE™ and PCM is ongoing, but is time-consuming and carries with it the risk of not yielding the desired results. Ultimately, the Defendants may not be able to obtain FDA clearance or approval of STRATAFIDE™ or PCM (or, in fact, any other IVD product).

245. PCM is intended to be a bespoke IVD product, and even if FDA approved, the composition and reaction conditions of the product that will be utilized is not presently known—the components will be developed on a patient-by-patient basis.

THIRD DEFENSE
(Non-Infringement)

246. The Defendants have not infringed, and are not infringing, literally or under the doctrine of equivalents, directly, or jointly, any valid and enforceable claim of any Asserted Patent.

247. For example, claim 1 of the '814 Patent recites "performing a first PCR...using a universal primer" and "performing a second, nested PCR...using the universal primer and at least 10 inner target-specific primers..., wherein at least one of the primers comprises a sequencing tag." ArcherDX's accused AMP™ process does not include "a second, nested PCR... using the universal primer" of the first PCR, nor does "at least one of the [universal primer and at least 10 inner target-specific primers] comprises a sequencing tag."

248. As another example, claim 1 of the '172 Patent recites "performing a first PCR...using a universal primer" and "performing a second, nested PCR...using the universal

primer." ArcherDX's accused AMP™ process does not include "a second, nested PCR... using the universal primer" of the first PCR.

249. As another example, claim 1 of the '482 Patent recites "performing a first PCR...using a universal primer" and "performing a second, nested PCR...using the universal

primer." ArcherDX's accused AMP™ process does not include "a second, nested PCR... using the universal primer" of the first PCR.

250. As another example, claim 1 of the '708 Patent recites "subjecting the reaction mixture to primer extension reaction conditions...; wherein the annealing temperature for the reaction conditions is greater than a melting temperature of the at least 2 primers." ArcherDX's accused AMP™ process does not include reaction conditions "wherein annealing temperature for the reaction conditions is greater than a melting temperature of the at least 2 primers."

251. As another example, claim 1 of the '220 Patent recites "performing a second, nested PCR...using a second universal primer and at least 10 inner target-specific primers..., wherein at least one of the primers comprises a sequencing tag." ArcherDX's accused AMP™ process does not include "a second, nested PCR...wherein at least one of the [second universal primer and at least 10 inner target-specific primers] comprises a sequencing tag."

252. Further, the Defendants have not infringed contributorily or by inducement any valid and enforceable claim of any Asserted Patent because there is no direct infringement; ArcherDX's accused AMP™ process does not fall within the claims of any Asserted Patent. Moreover, to the extent Natera asserts that the Defendants indirectly infringe any Asserted Patent, including by inducement of infringement, the Defendants are not liable because, at a minimum, the Defendants lack the requisite intent or knowledge to induce direct infringement of any Asserted Patent by another. The Defendants also lack the knowledge required for a finding of contributory infringement under 35 U.S.C. § 271(c).

FOURTH DEFENSE
(Safe Harbor)

253. Natera's patent infringement claims are barred in whole or in part because the alleged infringing activities fall within the safe harbor provision of 35 U.S.C. § 271(e)(1).

254. STRATAFIDE™ and PCM are in development for approval or clearance by the FDA.

255. Neither STRATAFIDE™ nor PCM is presently cleared or approved by the FDA—indeed applications for clearance or approval are not yet on file with the FDA. Both STRATAFIDE™ and PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products) require premarket approval or 510(k) approval or clearance to be sold commercially. Moreover, it is not act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention solely for uses reasonably related to the development and submission of information to the FDA for premarket approval or 510(k) approval or clearance of STRATAFIDE™ or PCM (or any other IVD oncology product in development and that utilizes the same technology as any of the Accused Products).

FIFTH DEFENSE
(Invalidity)

256. Each of the asserted claims of the Asserted Patents are invalid for failure to satisfy one or more conditions for patentability set forth under 35 U.S.C. including but not limited to §§ 101, 102, 103, and 112 et seq., and the rules, regulations, and laws pertaining to those provisions, including the applicable provisions of Title 37 of the Code of Federal Regulations.

257. The Asserted cfDNA Patents are invalid under 35 U.S.C. §§ 102 and/or § 103 in view of Mir, alone or in combination with additional prior art, including Wei-peng Wang et al., Multiplex Single Nucleotide Polymorphism Genotyping By Adapter Ligation-Mediated Allele-~~Specific~~ Specific Amplification, Analytical Biochemistry 355, 240–248 (2006) ("Wang"), Diego Spertini, Screening of Transgenic Plants by Amplification of Unknown Genomic DNA Flanking ~~T-DNA~~T-

DNA, 27 BioTechniques 308 (1999) ("Spertini") or U.S. Patent App. No. 2007/0031857

("Makarov"), which disclose all elements of the Asserted cfDNA Patents claims. Natera disclosed Mir as one of *thousands* of references during prosecution of the Asserted cfDNA Patents. Natera did not disclose either Wang, Spertini, or Makarov to the USPTO during prosecution of the Asserted cfDNA Patents. Moreover, the Asserted cfDNA Patents are at least obvious under 35 U.S.C. § 103 given Natera's own admissions made in court filings in this District and elsewhere, which are delineated below in the Defendants' Counterclaims.

258. The Asserted cfDNA Patents are also not entitled to a priority date earlier than their filing date of April 30, 2019, because Natera's provisional applications and earlier-filed applications do not comply with the requirements of 35 U.S.C § 112, as required by 35 U.S.C §§ 119 and 120.

259. The provisional applications and earlier-filed applications do not contain a written description of the claims of the Asserted cfDNA Patents or contain sufficient information to enable a person of ordinary skill in the art to which they pertain to practice the full scope of the claims of the Asserted cfDNA Patents.

260. Indeed, none of the provisional applications or earlier-filed applications disclosed or sought claims corresponding to the claims of the Asserted cfDNA Patents, which recite processes that Natera did not invent.

261. Because the Asserted cfDNA Patents are not entitled to a priority date earlier than their filing date of April 30, 2019, they are invalid under 35 U.S.C. §§ 102 and/or § 103 in further view of, for example, the following prior art, alone or in combination with additional prior art: U.S. Patent App. No. 2018/0127744 ("Hu") or International App. No. WO 2017/205540 ("Murtaza"), which disclose all elements of the Asserted cfDNA Patents claims. Natera did not disclose either Hu or Murtaza to the USPTO during prosecution of the Asserted cfDNA Patents.

Moreover, the Asserted cfDNA Patents are at least obvious under 35 U.S.C. § 103 given Natera's own admissions made in court filings in this District and elsewhere, which are delineated below in the Defendants' Counterclaims.

262. The Asserted '708 Patent is invalid under 35 U.S.C. §§ 102 and/or § 103 in view of Iafrate" or Rabinowitz, alone or in combination with additional prior art, which disclose all elements of the '708 Patent claims. Natera disclosed a related Iafrate application (U.S. Patent App. Pub. No. 2013/0303461) and Rabinowitz as two of *thousands* of references during prosecution of the '708 Patent. Moreover, the '708 Patent is at least obvious under 35 U.S.C. § 103 given Natera's own admissions made in court filings in this District and elsewhere, which are delineated below in the Defendants' Counterclaims.

263. The Asserted '708 Patent is also not entitled to a priority date earlier than its filing date of April 30, 2019, because Natera's provisional applications and earlier-filed applications do not comply with the requirements of 35 U.S.C § 112, as required by 35 U.S.C §§ 119 and 120.

264. The provisional applications and earlier-filed applications do not contain a written description of the claims of the '708 Patent or contain sufficient information to enable a person of ordinary skill in the art to which they pertain to practice the full scope of the claims of the '708 Patent.

265. Indeed, none of the provisional applications or earlier-filed applications disclosed or sought claims corresponding to the claims of the '708 Patent, which recite processes that Natera did not invent.

SIXTH DEFENSE
(Prosecution History Estoppel/Disclaimer)

266. Natera is estopped from construing the claims of the Asserted Patents to cover or include, either literally or by application of the doctrine of equivalents, products manufactured,

used, imported, sold, or offered for sale by the Defendants or methods used by the Defendants because of amendments, admissions, representations, or statements made before the USPTO during prosecution of the applications leading to the issuance of the Asserted Patents or applications related thereto, because of disclosures or language in the specifications of the Asserted Patents, and/or because of limitations in the claims of the Asserted Patents.

SEVENTH DEFENSE
(Limitations on Recovery)

267. Natera's claims for damages and other remedies are limited by 35 U.S.C. §§ 286 and/or 288. Natera is barred by 35 U.S.C. § 288 from recovering costs associated with this action.

EIGHTH DEFENSE
(Barring of Claims for Injunctive Relief)

268. Natera is not entitled to injunctive relief against the Defendants because any alleged injury are not immediate or irreparable, Natera has an adequate remedy at law for its alleged injury, the balance of hardships does not favor an injunction, and the public interest would be disserved by an injunction. For example, enjoining the Defendants would have significant negative impacts on public health and welfare, and would disrupt important medical research. Indeed, the Defendants' products have the potential to significantly advance cancer care.

NINTH DEFENSE
(License and/or Exhaustion)

269. To the extent that any of the allegedly infringing activities is directly or indirectly related to or based on products made, sold, or provided by, or services conducted by an entity that has an express or implied license to the Asserted Patents, or to the extent that any of the allegedly infringing conduct is directly or indirectly subject to rights granted to the Defendants or another entity, Natera's claims are barred, in whole or in part, in view of such licensed rights, implied or otherwise, covenant not to sue, and/or under the doctrine of patent exhaustion.

TENTH DEFENSE
(No Standing)

270. To the extent Natera does not have title to the Asserted Patents, Natera has no standing to maintain its claims.

ELEVENTH DEFENSE
(Actions of Others)

271. On information and belief, Natera's claims are barred, in whole or in part, because the Defendants are not liable for the acts of others over whom they have no control.

TWELFTH DEFENSE
(No Exceptional Case)

272. Natera cannot prove that this is an exceptional case that justifies an award of attorney fees against the Defendants pursuant to 35 U.S.C. § 285.

THIRTEENTH DEFENSE
(Unclean Hands)

273. Natera's patent infringement claims are barred in whole or in part under the doctrine of unclean hands.

The '814 Patent and the '172 Patent

274. As particularized below, the '814 Patent and the '172 Patent are the results of protracted and convoluted prosecution at the USPTO spanning more than a decade, and involving 16 provisional patent applications and 10 continuation or continuation-in-part applications, almost half of which were abandoned.

275. The '814 Patent and the '172 Patent are continuations of U.S. Patent App. No. 16/140,298 filed September 24, 2018.

276. U.S. Patent App. No. 16/140,298 is a continuation of U.S. Patent App. No. 14/918,544, filed October 20, 2015.

277. U.S. Patent App. No. 14/918,544 is a continuation-in-part of U.S. Patent App. No. 14/877,925, filed October 7, 2015, which is now abandoned; a continuation-in-part of U.S. Patent App. No. 14/692,703, filed April 21, 2015; and a continuation-in-part of U.S. Patent App. No. 14/538,982. U.S. Patent App. No. 14/918,544 claims priority to U.S. Provisional App. No. 62/147,377, filed April 14, 2015; U.S. Provisional App. No. 62/146,188, filed April 10, 2015; and U.S. Provisional App. No. 62/066,514, filed October 21, 2014.

278. U.S. Patent App. No. 14/877,925 is a continuation-in-part of U.S. Patent App. No. 14/255,356, filed March 25, 2014, which is now abandoned after the applicant failed to respond to any office action in prosecution; a continuation-in-part of U.S. Patent App. No. 13/780,022, filed February 28, 2013, which is now abandoned; and a continuation of U.S. Patent App. No. 13/683,604, filed November 21, 2012, which is now abandoned.

279. U.S. Patent App. No. 14/692,703 claims priority to U.S. Provisional App. No. 62/148,173, filed April 15, 2015; U.S. Provisional App. No. 62/147,377, filed April 14, 2015; U.S. Provisional App. No. 62/146,188, filed April 10, 2015; U.S. Provisional App. No. 62/066,514, filed October 21, 2014; U.S. Provisional App. No. 61/994,791, filed May 16, 2014; U.S. Provisional App. No. 61/987,407, filed May 1, 2014; and U.S. Provisional App. No. 61/982,245, filed April 21, 2014.

280. U.S. Patent App. No. 14/538,982 claims priority to U.S. Provisional App. No. 62/066,514, filed October 21, 2014; U.S. Provisional App. No. 61/994,791, filed May 16, 2014; U.S. Provisional App No. 61/987,407, filed May 1, 2014; and U.S. Provisional App. No. 61/982,245, filed April 21, 2014.

281. U.S. Patent App. No. 14/255,356 is a continuation of PCT Application PCT/US2012/58578, filed October 3, 2012.

282. U.S. Patent App. No. 13/780,022 is a continuation-in-part of U.S. Patent App. No. 13/683,604, filed November 21, 2012, which is now abandoned; a continuation-in-part of PCT Application No. PCT/US2012/58578, filed October 3, 2012; a continuation-in-part of U.S. App. No. 13/335,043, filed December 22, 2011; a continuation-in-part of U.S. Patent App. No. 13/300,235, filed November 18, 2011; and a continuation-in-part of U.S. App. No. 13/110,685, filed May 18, 2011; and claims priority to U.S. Provisional App. No. 61/634,431, filed February 29, 2012.

283. U.S. Patent App. No. 13/683,604 is a continuation-in-part of U.S. Patent App. No. 13/300,235, filed November 18, 2011; a continuation-in-part of U.S. App. No. 13/110,685, filed May 18, 2011; and claims priority to U.S. Provisional App. No. 61/675,020, filed July 24, 2012.

284. PCT Application PCT/US2012/58578 is a continuation-in-part of U.S. Patent App. No. 13/300,235, filed November 18, 2011; and claims priority to U.S. Provisional App. No. 61/683,331, filed August 15, 2012; and U.S. Provisional App. No. 61/542,508, filed October 3, 2011.

285. U.S. Patent App. No. 13/335,043 is a continuation-in-part of U.S. Patent App. No. 13/300,235, filed November 18, 2011; a continuation-in-part of U.S. Patent App. No. 13/110,685, filed May 18, 2011; and claims priority to U.S. Provisional App. No. 61/426,208, filed December 22, 2010.

286. U.S. Patent App. No. 13/300,235 is a continuation-in-part of U.S. Patent App. No. 13/110,685, filed May 18, 2011; and claims priority to U.S. Provisional App. No. 61/542,508, filed October 3, 2011; and U.S. Provisional App. No. 61/571,248, filed June 23, 2011.

287. U.S. Patent App. No. 13/110,685 claims priority to U.S. Provisional App. No 61/516,996, filed April 12, 2011; U.S. Provisional App. No. 61/448,547, filed March 2, 2011; U.S. Provisional App. No. 61/462,972, filed February 9, 2011; U.S. Provisional App. No. 61/398,159, filed June 21, 2010; and U.S. Provisional App. No. 61/395,850, filed May 18, 2011.

288. In connection with the above applications, Natera filed hundreds of proposed claims with the USPTO.

289. Prior to the filing of the ’814 Patent application and the ’172 Patent application on April 30, 2019, Natera had never disclosed nor sought claims corresponding to the claims of the ’814 Patent or ’172 Patent.

290. On information and belief, Natera drafted the claims of the ’814 Patent and the ’172 Patent in an egregious attempt to cover ArcherDX’s proprietary AMP™ process—a method of amplifying DNA that Natera did not invent.

291. Indeed, Natera filed the ’814 and the ’172 Patent applications only after one of its senior executives left Natera, began working for ArcherDX, gained access to confidential information relating to ArcherDX’s Accused Products and then returned to Natera.

The ’482 Patent

292. As particularized below, the ’482 Patent is the result of protracted and convoluted prosecution at the USPTO spanning close to a decade, and involving 8 provisional patent applications and 4 continuation or continuation-in-part applications.

293. The ’482 Patent is a continuation of U.S. Patent App. No. 16/012,667 filed June 19, 2018.

294. U.S. Patent App. No. 16/012,667 is a continuation of U.S. App. No. 13/335,043, filed December 22, 2011; a continuation-in-part of U.S. Patent App. No. 13/300,235, filed November 18, 2011; and a continuation-in-part of U.S. App. No. 13/110,685, filed May 18, 2011.

295. U.S. Patent App. No. 13/335,043 is a continuation-in-part of U.S. Patent App. No. 13/300,235, filed November 18, 2011; a continuation-in-part of U.S. Patent App. No. 13/110,685, filed May 18, 2011; and claims priority to U.S. Provisional App. No. 61/426,208, filed December 22, 2010.

296. U.S. Patent App. No. 13/300,235 is a continuation-in-part of U.S. Patent App. No. 13/110,685, filed May 18, 2011; and claims priority to U.S. Provisional App. No. 61/542,508, filed October 3, 2011; and U.S. Provisional App. No. 61/571,248, filed June 23, 2011.

297. U.S. Patent App. No. 13/110,685 claims priority to U.S. Provisional App. No. 61/516,996, filed April 12, 2011; U.S. Provisional App. No. 61/448,547, filed March 2, 2011; U.S. Provisional App. No. 61/462,972, filed February 9, 2011; U.S. Provisional App. No. 61/398,159, filed June 21, 2010; and U.S. Provisional App. No. 61/395,850, filed May 18, 2011.

298. In connection with the above applications, Natera filed hundreds of proposed claims with the USPTO.

299. Prior to the filing of the ’482 Patent application on April 30, 2019, Natera had never disclosed nor sought claims corresponding to the claims of the ’482 Patent.

300. On information and belief, Natera drafted the claims of the ’482 Patent in an egregious attempt to cover ArcherDX’s proprietary AMP™ process—a method of amplifying DNA that Natera did not invent.

301. Indeed, Natera filed the ’482 Patent application only after one of its senior executives

left Natera, began working for ArcherDX, gained access to confidential information relating to ArcherDX's Accused Products and then returned to Natera.

The '708 Patent

302. As particularized below, the '708 Patent is the result of protracted and convoluted prosecution at the USPTO for close to 6 years, and involving multiple provisional and continuation patent applications.

303. The '708 Patent is a continuation of U.S. Patent App. No. 15,336,630 filed October 27, 2016; a continuation of application No. 14/538,982, filed on November 24, 2014.

304. U.S. Patent App. No. 14/538,982 claims priority to U.S. Provisional App. No. 62/066,514, filed October 21, 2014; U.S. Provisional App. No. 61/994,791, filed May 16, 2014; U.S. Provisional App. No. 61/987,407, filed May 1, 2014; and U.S. Provisional App. No. 61/982,245, filed April 21, 2014.

305. Prior to the filing of the '708 Patent application on April 30, 2019, Natera had never disclosed nor sought claims corresponding to the claims of the '708 Patent.

306. On information and belief, Natera drafted the claims of the '708 Patent in an egregious attempt to cover ArcherDX's proprietary AMP™ process—a method of amplifying nucleic acids that Natera did not invent.

307. Indeed, Natera filed the '708 Patent application only after one of its senior executives left Natera, began working for ArcherDX, gained access to confidential information relating to ArcherDX's Accused Products and then returned to Natera.

308. Moreover, on information and belief, Natera knew or should have known that the Asserted Patents are invalid under at least 35 U.S.C. §§ 101 and 103 given Natera's own

admissions made in court filings in this District and elsewhere, representative examples of which are set forth below in ArcherDX's Counterclaims.

309. On information and belief, Natera has improperly sought to delay competition in the IVD market by pursuing patent claims it did not invent, and subsequently prematurely asserting invalid patents that do not cover ArcherDX's products in development.

310. Based on the foregoing business misconduct, the relief Natera seeks in this action is barred by reason of its unclean hands.

The '220 Patent

311. Natera's patent infringement claims are barred in whole or in part under the doctrine of unclean hands.

312. As particularized below, the '220 Patent is the result of protracted and convoluted prosecution at the USPTO spanning more than a decade, and involving 16 provisional patent applications and 11 continuation or continuation-in-part applications, almost half of which were abandoned.

313. The '220 Patent is a continuation of U.S. Patent App. No 16/399,268 filed April 30, 2019.

314. U.S. Patent App. No. 16/399,268 is a continuation of U.S. Patent App. No. 16/140,298 filed September 24, 2018.

315. U.S. Patent App. No. 16/140,298 is a continuation of U.S. Patent App. No. 14/918,544, filed October 20, 2015.

316. U.S. Patent App. No. 14/918,544 is a continuation-in-part of U.S. Patent App. No. 14/877,925, filed October 7, 2015, which is now abandoned; a continuation-in-part of U.S. Patent App. No. 14/692,703, filed April 21, 2015; and a continuation-in-part of U.S. Patent App.

No. 14/538,982. U.S. Patent App. No. 14/918,544 claims priority to U.S. Provisional App.

No. 62/147,377, filed April 14, 2015; U.S. Provisional App. No. 62/146,188, filed April 10, 2015; and U.S. Provisional App. No. 62/066,514, filed October 21, 2014.

317. U.S. Patent App. No. 14/877,925 is a continuation-in-part of U.S. Patent App. No. 14/255,356, filed March 25, 2014, which is now abandoned after the applicant failed to respond to any office action in prosecution; a continuation-in-part of U.S. Patent App. No. 13/780,022, filed February 28, 2013, which is now abandoned; and a continuation of U.S. Patent App. No. 13/683,604, filed November 21, 2012, which is now abandoned.

318. U.S. Patent App. No. 14/692,703 claims priority to U.S. Provisional App. No. 62/148,173, filed April 15, 2015; U.S. Provisional App. No. 62/147,377, filed April 14, 2015; U.S. Provisional App. No. 62/146,188, filed April 10, 2015; U.S. Provisional App. No. 62/066,514, filed October 21, 2014; U.S. Provisional App. No. 61/994,791, filed May 16, 2014; U.S. Provisional App. No. 61/987,407, filed May 1, 2014; and U.S. Provisional App. No. 61/982,245, filed April 21, 2014.

319. U.S. Patent App. No. 14/255,356 is a continuation of PCT Application PCT/US2012/58578, filed October 3, 2012.

320. U.S. Patent App. No. 13/780,022 is a continuation-in-part of U.S. Patent App. No. 13/683,604, filed November 21, 2012, which is now abandoned; a continuation-in-part of PCT Application No. PCT/US2012/58578, filed October 3, 2012; a continuation-in-part of U.S. App. No. 13/335,043, filed December 22, 2011; a continuation-in-part of U.S. Patent App. No. 13/300,235, filed November 18, 2011; and a continuation-in-part of U.S. App. No. 13/110,685, filed May 18, 2011; and claims priority to U.S. Provisional App. No. 61/634,431, filed February 29, 2012.

321. U.S. Patent App. No. 13/683,604 is a continuation-in-part of U.S. Patent App. No. 13/300,235, filed November 18, 2011; a continuation-in-part of U.S. App. No. 13/110,685, filed May 18, 2011; and claims priority to U.S. Provisional App. No. 61/675,020, filed July 24, 2012.

322. PCT Application PCT/US2012/58578 is a continuation-in-part of U.S. Patent App. No. 13/300,235, filed November 18, 2011; and claims priority to U.S. Provisional App. No. 61/683,331, filed August 15, 2012; and U.S. Provisional App. No. 61/542,508, filed October 3, 2011.

323. U.S. Patent App. No. 13/335,043 is a continuation-in-part of U.S. Patent App. No. 13/300,235, filed November 18, 2011; a continuation-in-part of U.S. Patent App. No. 13/110,685, filed May 18, 2011; and claims priority to U.S. Provisional App. No. 61/426,208, filed December 22, 2010.

324. U.S. Patent App. No. 13/300,235 is a continuation-in-part of U.S. Patent App. No. 13/110,685, filed May 18, 2011; and claims priority to U.S. Provisional App. No. 61/542,508, filed October 3, 2011; and U.S. Provisional App. No. 61/571,248, filed June 23, 2011.

325. U.S. Patent App. No. 13/110,685 claims priority to U.S. Provisional App. No 61/516,996, filed April 12, 2011; U.S. Provisional App. No. 61/448,547, filed March 2, 2011; U.S. Provisional App. No. 61/462,972, filed February 9, 2011; U.S. Provisional App. No. 61/398,159, filed June 21, 2010; and U.S. Provisional App. No. 61/395,850, filed May 18, 2011.

326. In connection with the above applications, Natera filed hundreds of proposed claims with the USPTO.

327. Prior to the filing of the '220 Patent application on January 15, 2020, Natera had never disclosed methods nor sought claims corresponding to the claims of the '220 Patent.

328. On information and belief, Natera drafted the claims of the '220 Patent in an egregious attempt to cover ArcherDX's proprietary AMP™ process—a method of amplifying DNA that Natera did not invent.

329. Indeed, Natera filed the '220 Patent application only after one of its senior executives left Natera, began working for ArcherDX, gained access to confidential information relating to ArcherDX's Accused Products and then returned to Natera.

330. Moreover, on information and belief, Natera knew or should have known that the Asserted Patent is invalid under at least 35 U.S.C. §§ 101 and 103 given Natera's own admissions made in court filings in this District and elsewhere, representative examples of which are set forth below in ArcherDX's Counterclaims.

331. On information and belief, Natera has improperly sought to delay competition in the IVD market by pursuing patent claims it did not invent, and subsequently prematurely asserting invalid patents that do not cover ArcherDX's products in development.

332. Based on the foregoing business misconduct, the relief Natera seeks in this action is barred by reason of its unclean hands.

FOURTEENTH DEFENSE
(Prosecution Laches)

333. Natera's patent infringement claims are barred in whole or in part under the doctrine of prosecution laches.

334. As described above, on information and belief, Natera engaged in an unreasonable and undue delay in the prosecution of the Asserted Patents, which have prejudiced the Defendants. Thus, as a matter of equity, the Asserted Patents cannot be enforced against the Defendants.

FIFTEENTH DEFENSE
(~~Prosecution Laches~~Inequitable Conduct)

335. The '220, '172, '482, and '814 ~~P~~patents ~~is~~are unenforceable due to Natera's

inequitable conduct during prosecution of these patents.

~~prosecution of the '220 Patent.~~

336. On information and belief, Dr. Matthew Rabinowitz is the Executive Chairman, founder, and former-CEO of Natera, as well as a named inventor on the '220 Patent. Dr. Rabinowitz had a general duty of candor and good faith in his dealings with the USPTO. Pursuant to 37 C.F.R. § 1.56, an inventor has an affirmative obligation to disclose to the USPTO all information known to be material to the examination of a pending patent application. On January 15, 2020, in connection with the application that led to the '220 Patent, Dr. Rabinowitz filed an Inventor's Oath or Declaration with the USPTO pursuant to 37 C.F.R. § 1.63, acknowledging that he was "aware of the duty to disclose to the Office all information known to the person to be material to patentability."

337. According to Natera's Form 10-Q for the quarterly period ended June 30, 2020 dated August 6, 2020, "Dr. Rabinowitz spends significant time with [Natera] and is active in [Natera's] management." Ex. 14 at 68; *see also id.* at 67-68 ("If we lose the services of our founder and Executive Chairman or other members of our senior management team, we may not be able to execute our business strategy.").

338. On information and belief, as a named inventor on the patents in dispute and the Executive Chairman of Natera and someone active in Natera's management, Dr. Rabinowitz was aware of the ongoing action between Natera and ArcherDX captioned *Natera, Inc., v. ArcherDX, Inc.*, No. 1:20-cv-125 (D. Del.), including (1) ArcherDX's Answer filed on March 25, 2020 (D.I. 14) ("Answer"), (2) ArcherDX's Answer to the First Amended Complaint filed on May 13,

2020 (D.I. 21) ("Answer to FAC"), (3) ArcherDX's Opening Brief in Support of its Motion for

Judgment on the Pleadings filed on June 4, 2020 (D.I. 24) ("12(c) Motion"), and (4) ArcherDX's Reply Brief in Support of its Motion for Judgment on the Pleadings filed on July 30, 2020 (D.I. 24) ("12(c) Reply"). On information and belief, by reason of his position as an inventor and the Executive Chairman of Natera and as someone active in Natera's management, Dr. Rabinowitz knew of the arguments set forth in these filings while the '220 Patent was still in prosecution before the USPTO.

339. ArcherDX, Inc.'s Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply set forth invalidity arguments under 35 U.S.C. §§ 101, 103, and 112 for patents closely related to the Asserted Patent, including U.S. Patent No. 10,538,814 (the "'814 Patent") of which the Asserted Patent is a continuation, and on which Dr. Rabinowitz is also named as an inventor.

340. ArcherDX Inc.'s Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply set forth arguments that the '814 Patent, which is directed to the same unpatentable matter as the '220 Patent, is not patentable under § 101. For example, they set forth that claims directed to a "method of amplifying and sequencing" cell-free DNA comprising (1) ligating adaptors to cell free DNA, (2) performing a first round of PCR, (3) performing a second round of nested PCR, and (4) performing high-throughput sequencing are directed to unpatentable subject matter. *See* 12(c) Motion at 13-15 ("The asserted claims begin with naturally occurring cfDNA and, after amplification and detection, end with the same genetic information; the purpose of the claim is to detect."); 12(c) Reply at 8; Answer to FAC at Counterclaims ¶¶ 17-22. The Answer, Answer to

FAC, 12(c) Motion, and 12(c) Reply set forth that such claims are directed to the natural phenomenon of detecting cell-free DNA and utilize well-known techniques of amplification and sequencing. *See* 12(c) Motion at 16-19 ("[T]he claims recite the use of generic, well-known elements such as 'primers,' 'adaptors,' and 'sequencing tags' for use in conventional and routine

'PCR' and 'high-throughput sequencing.'"); 12(c) Reply at 9-10; Answer to FAC at Counterclaims ¶¶ 17-22. Further, they highlighted statements made by Natera in other litigation arguing the same. *See* 12(c) Motion at 16-18 ("Natera's admissions readily show that each method step was routine."); 12(c) Reply at 9-10; Answer to FAC at ¶ 37.

341. ArcherDX's Answer and Answer to FAC set forth arguments that the '814 Patent, which claims highly similar methods to the '220 Patent, is invalid under § 103. For example, they set forth that the prior art of Mir alone or Mir in a specific combination with Wang, Spertini, or Makarov, discloses all elements of the '814 Patent claims. *See* Answer to FAC at Counterclaims ¶¶ 23-25. The Answer and Answer to FAC also set forth that Mir disclosed the elements that the USPTO's examiner mistakenly stated were not in the prior art, such as, the "amplification of . . . circulating nucleic acids," "sequencing steps, . . . incorporat[ing] a universal or common primer, and . . . a sequencing tag," and "'nested PCR' following the recited 'first PCR of 'cell-free DNA.'" *See id.* at ¶ 37, 44. The Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply also highlighted statements made by Natera in other litigation describing claim elements as routine and conventional and, hence, part of the state of the art and within the person of ordinary skill in the art's skill. *See* 12(c) Motion at 16-18 ("Natera's admissions readily show that each method step was routine."); 12(c) Reply at 9-10; Answer to FAC at ¶ 37.

342. ArcherDX Inc.'s Answer and Answer to FAC set forth arguments that the '814 Patent is invalid under § 112. For example, they set forth that the '814 Patent, which shares a

specification with the '220 Patent, does not disclose (a) an embodiment corresponding to the claimed methods, (b) that the named inventors were in possession of the alleged invention, or (c) sufficient information to enabled a person of ordinary skill in the art to practice the claims. *See*

Answer to FAC at Counterclaims ¶¶ 26-31. The Answer and Answer to FAC set forth that the claims were not entitled to a priority date earlier than the filing date. *See id*. at Counterclaims ¶ 25.

343. On information and belief, as the Executive Chairman of Natera and someone active in Natera's management, Dr. Rabinowitz was also aware of the ongoing action between Natera and CareDX captioned *CareDX, Inc. et al. v. Natera, Inc.*, No. 19-cv-567 (D. Del.), including (1) Natera's Reply in Support of Motion to Dismiss filed on June 24, 2019 (D.I. 19), (2) Natera's Objections to Report and Recommendations filed on February 24, 2020 (D.I. 63), (3) Natera's Opening Brief in Support of Renewed Motion to Dismiss filed on April 9, 2020 (D.I. 87), (4) Natera's Opening Brief in Support of Summary Judgment of Invalidity filed on June 11, 2020 (D.I. 101), and (5) Natera's Statement re Motion for Summary Judgment of Invalidity filed on June 11, 2020 (D.I. 102) (collectively, "CareDX Briefing"). On information and belief, by reason of his position as the Executive Chairman of Natera and as someone active in Natera's management, Dr. Rabinowitz knew of Natera's own arguments set forth in these filings while the '220 Patent was still in prosecution before the USPTO.

344. Natera's CareDX Briefing sets forth arguments for invalidity under 35 U.S.C. § 101 for patents claiming methods of detecting cell-free DNA, including statements of what was "routine" and "conventional" as of 2009 and 2010, prior to the earliest possible priority date for the claims of the '220 Patent.

345. On information and belief, as the Executive Chairman of Natera and someone active in Natera's management, Dr. Rabinowitz was aware of the action between Natera and

Illumina, captioned *Illumina, Inc. v. Natera, Inc.*, No. 18-cv-01662 (N.D. Cal.), including (1) Natera's Motion to Dismiss filed May 17, 2018 (D.I. 24), and (2) Natera's Reply in Support of Motion to Dismiss filed June 7, 2018 (D.I. 35) (collectively, "Illumina Briefing"). On information

and belief, by reason of his position as the Executive Chairman of Natera and as someone active in Natera's management, Dr. Rabinowitz knew of Natera's own arguments set forth in these filings while the '220 Patent was still in prosecution before the USPTO.

346. Natera's Illumina Briefing sets forth arguments for invalidity under 35 U.S.C. § 101 for a patent claiming methods of amplifying and sequencing DNA, including statements of what was "routine" and "conventional" as of 2010, prior to the earliest possible priority date for the claims of the '220 Patent.

347. Despite knowing of the arguments set forth in ArcherDX Inc.'s Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply, as well as Natera's CareDX Briefing and Natera's Illumina Briefing, Dr. Rabinowitz failed to disclose any of these documents to the USPTO during prosecution of the '220 Patent.

348. Dr. Rabinowitz's failure to disclose these documents to the USPTO was but-for material to the issuance of the '220 Patent. If the USPTO had been made aware of these documents setting forth arguments for invalidity under §§ 101, 103, and 112, the '220 Patent would not have issued.

349. As set forth in the Defendants' Counterclaims filed herewith (¶¶ 17-22), the arguments presented in ArcherDX Inc.'s Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply, as well as Natera's statements made in the Illumina Briefing and the CareDX Briefing establish that the claims of the '220 Patent are unpatentable under § 101 (and, as detailed below, support a finding that these claims are obvious). For example, Archer's 12(c) motion includes the following

table highlighting Natera's admissions that elements of the '814 Patent, which correspond to elements of the '220 Patent, are routine or conventional:

'814 Claim Language	Natera Admissions
1. A method for amplifying and sequencing DNA, comprising:	
ligating adaptors to cell free DNA isolated from a biological sample, wherein the adaptors each comprises a universal priming site;	"The DNA in the sample may have **ligation adapters**... appended, wherein **the ligation adapters contain a universal priming sequence**, followed by a universal amplification... this may be done **using a *standard protocol* designed to create sequencing libraries**." '814 Patent, 94:11-16.
performing a first PCR to simultaneously amplify at least 10 target loci using a universal primer and at least 10 target specific primers in a single reaction volume;	"The specification lists several **well known PCR techniques** that can be used to carry out the claimed method, such as '... **multiplex PCR.**'" Illumina Mot., 7. "**Primers routinely** are used in these amplification methods to bind to the **regions of a DNA strand where the DNA sequences of interest are located.**" Illumina Mot., 7. "Universal amplification of DNA using ligated adaptors **with primers specific to the adaptor tags**,... has the effect of enriching the proportion of shorter DNA strands... [E]xample protocols **are published and well known to those in the art**." '814 Patent, 212:14-21. "In some embodiments [the commercially available] QIAGEN **Multiplex PCR Kit** is used..." '814 Patent, 235:15-16.
performing a second, nested PCR to simultaneously amplify the at least 10 target loci using the universal primer and at least 10 inner target specific primers in a single reaction volume,	(Same as above) "[R]unning **multiple cycles of amplification** to copy DNA sequences was **routine and conventional**." Illumina Reply, 7. "The specification lists several **well known PCR techniques**... such as... multiplex PCR, or **nested PCR**." Illumina Mot., 7.
wherein at least one of the primers comprises a sequencing tag;	"It is also **routine and conventional** in the art to attach to the primers what are known as **sequence 'tag[s].**'" Illumina Mot., 7.
'814 Claim Languageperforming high throughput sequencing to sequence the amplified DNA comprising the target loci.	"[T]he asserted claims recite nothing more than **conventional techniques**, such as... **high throughput sequencing**." CareDX Reply, 6-7.**Natera Admissions**

1. A method for amplifying and sequencing DNA, comprising:	
ligating adaptors to cell-free DNA isolated from a biological sample, wherein the adaptors each comprises a universal priming site;	"The DNA in the sample may have **ligation adapters**... appended, wherein **the ligation adapters contain a universal priming sequence**, followed by a universal amplification... this may be done **using a *standard protocol* designed to create sequencing libraries**." '814 Patent, 94:11-16.
performing a first PCR to simultaneously amplify at least 10 target loci using a universal primer and at least 10 target-specific primers in a single reaction volume;	"The specification lists several **well-known PCR techniques** that can be used to carry out the claimed method, such as '... **multiplex PCR.**'" Illumina Mot., 7. "**Primers routinely** are used in these amplification methods to bind to the **regions of a DNA strand where the DNA sequences of interest are located.**" Illumina Mot., 7. "Universal amplification of DNA using ligated adaptors **with primers specific to the adaptor tags**,... has the effect of enriching the proportion of shorter DNA strands... [E]xample protocols **are published and well known to those in the art**." '814 Patent, 212:14-21. "In some embodiments [the commercially available] QIAGEN **Multiplex PCR Kit** is used..." '814 Patent, 235:15-16.
performing a second, nested PCR to simultaneously amplify the at least 10 target loci using the universal primer and at least 10 inner target-specific primers in a single reaction volume,	(Same as above) "[R]unning **multiple cycles of amplification** to copy DNA sequences was **routine and conventional**." Illumina Reply, 7. "The specification lists several **well-known PCR techniques**... such as... multiplex PCR, or **nested PCR**." Illumina Mot., 7.
wherein at least one of the primers comprises a sequencing tag;	"It is also **routine and conventional** in the art to attach to the primers what are known as **sequence 'tag[s].**'" Illumina Mot., 7.
performing high-throughput sequencing to sequence the amplified DNA comprising the target loci.	"[T]he asserted claims recite nothing more than **conventional techniques**, such as... **high throughput sequencing**." CareDX Reply, 6-7.

If Dr. Rabinowitz had disclosed these documents to the USPTO, the USPTO would not have issued the claims.

350. As set forth in the Defendants' Counterclaims filed herewith (¶¶ 23-25), the arguments presented in ArcherDX Inc.'s Answer and Answer to FAC establish that the claims of the '220 Patent are invalid as obvious under § 103. For example, ArcherDX Inc.'s Answer and Answer to the FAC disclose that the elements of the claims of the '220 Patent that the USPTO's examiner concluded were missing from the prior art, namely "multiplex using universal or common primers and a second step of nested amplification on the same multiplex amplified targets," are indeed disclosed in the prior art, including in Mir. Archer DX's Answer ¶ 31; ArcherDX Inc.'s Answer to FAC ¶¶ 37, 44. While Natera disclosed Mir to the USPTO, it was buried in thousands of references disclosed during prosecution of the '220 Patent. By way of another example, ArcherDX Inc.'s Answer and Answer to the FAC highlighted statements made by Natera in other litigations describing elements found in the '220 Patent claims as routine and conventional. Archer DX Inc.'s Answer ¶ 31; ArcherDX's Answer to FAC ¶¶ 37. Archer's 12(c) Motion and 12(c) Reply further highlight specific admissions by Natera that the elements of the claims of the '220 Patent that the examiner concluded were missing from the prior art were routine and conventional prior to the earliest claimed priority of the '220 Patent. *See* 12(c) Motion at 1618 ("The specification lists several well-known PCR techniques... such as... nested PCR" and "It is also routine and conventional in the art to attach to the primers what are known as sequence 'tag[s].'"); *see also* 12(c) Reply at 9. If Dr. Rabinowitz had disclosed these documents to the USPTO, the USPTO would not have issued the claims.

351. As set forth in the Defendants' Counterclaims filed herewith (¶¶ 26-31), the arguments presented in ArcherDX's Answer and Answer to FAC establish that the claims of the

'220 Patent are invalid under § 112 for lack of written description and enablement. If

Dr. Rabinowitz had disclosed these documents to the USPTO, the USPTO would not have issued the claims.

352. Upon information and belief, Dr. Rabinowitz knew that he had a duty to disclose these documents to the USPTO. Indeed, some litigation documents, including some filings from the Illumina action, were disclosed to the USPTO during prosecution of the '220 Patent. For example, Natera's "Motion to Dismiss" and "Opening Brief in Support of Motion to Dismiss" filed on May 16, 2019, briefing related to its motion to dismiss under 35 U.S.C. § 101, in the Illumina action was disclosed to the USPTO during prosecution. Moreover, Natera's "First Amended Answer, Affirmative Defenses and Counterclaims" filed August 16, 2018, its Answer in the Illumina action, was also disclosed to the USPTO during prosecution. These disclosures show that, as the Executive Chairman of Natera and someone active in Natera's management, Dr. Rabinowitz understood that Answers and briefing related to § 101 motions can be material to patentability and must be disclosed to the USPTO. Despite this, Dr. Rabinowitz failed to disclose any of the documents described above (¶¶ 197-205) that are material to patentability. The single most reasonable inference able to be drawn from these facts is that Dr. Rabinowitz's failure to disclose was the result of a specific intent to deceive the USPTO.

353. Dr. Rabinowitz engaged in inequitable conduct in the prosecution of the Asserted Patent. Thus, the Asserted Patent is unenforceable.

354. The '220, '814, '172, and '482 patents are further unenforceable due to inequitable conduct in connection with Natera's June 25, 2021 submissions of documents to the patent office to alter the named inventors on these patents.

355. In these June 25 filings, Natera made major changes to the patent inventorship group, including in some cases adding Johan Baner, Milena Banjevic, Allison Ryan, and Zachary

Demko as named inventors and removing Joshua Babiarz, Tudor Constantin, Lane Eubank, Huseyin Kirkizlar, and Onur Sakarya as named inventors.

356. Natera's change of inventorship was done with deceptive intent to name on the patents a false inventorship group consisting solely of individuals who worked at Natera in a time frame consistent with the October 2011 priority date upon which Natera wishes to rely upon in this case to avoid prior art.

357. By removing as inventors several individuals that were not even affiliated with Natera until long after Natera's desired invention date and adding individuals who were, Natera seeks to avoid any inference that its alleged invention post-dates the prior art relied upon in this case by Defendants. Indeed, in connection with its attempt to correct inventorship Natera failed to submit to the Patent Office Defendants' invalidity contentions and failed to notify the Patent Office of the serious questions regarding Natera's priority claim and invention date that have been raised in the instant litigation.

358. For example, Defendants' April 2021 invalidity contentions disputed Natera's priority claim. *See, e.g.*, Ex. 9 at 4-6, 44-48. Accordingly, Defendants relied upon several highly relevant prior art references post-dating the October 2011 invention date upon which Natera now seeks to rely, including work done at Massachusetts General Hospital

359. What's more, Defendants informed Natera of the inconsistency between Natera's allegations of conception and its inventorship group as early as January 2021:

> Across Natera's five asserted patents, there are 17 different named inventors, including several individuals who did not work at the company until long after the filing of the 2010 applications to which Natera's patents claim priority.

D.I. 107 at 1.

360. Defendants did so again in March 2021:

> What's more, of these five listed inventors, at least four only started working at Natera long after Natera's alleged conception date of November 18, 2011. For example, based on social media profiles, Joshua Babiarz started at Natera in December 2012, Tudor Constantin in 2013, and Lane Eubank and Onur Sakarya in 2014. See Exs. C–F. It appears that Natera has systematically excluded from its inventorship contentions any individual who started working at Natera after the date that Natera now wishes to rely upon for conception. When one considers the lack of substance in Natera's non-asserted dependent claims, there is thus a major inconsistency between Natera's original representations to the Patent Office about who the inventors are and the position Natera is now taking in this case. This casts considerable doubt upon Natera's claims that the inventions of the asserted claims were truly made by November 18, 2011.

D.I. 160 at 2.

361. Three months later, when Natera sought to correct inventorship, it did not inform the Patent Office of these inconsistencies, confirming that Natera's submissions to change inventorship on the '220, '482, '172, and '841 patents were made with deceptive intent. The individuals at Natera responsible for this attempt to improperly change the inventorship group include at least Anton Bokal, Tianran Yan, Matthew Rabinowitz, Bernhard Zimmerman, George Gemelos, and Zachary Demko.

362. The deposition testimony of the several originally named inventors taken to date confirms that Natera's recent change of inventorship was done with deceptive intent.

363. Natera's senior director of scientific communications and clinical research, Zachary Demko, was head of intellectual property and a patent agent at Natera during the time frame when Natera allegedly made the inventions of the '220, '482, '172, and '841 patents. According to Dr. Demko, Natera is careful and takes steps to make sure that Natera names the right inventors on its patent applications when it seeks patent protection. *See* Ex. 10 at 105:7-109:17. Likewise, Tudor Constantin confirmed that he consulted with Natera attorneys before originally being named as an inventor on the patent. *See* Ex. 11 at 103:11-104:13, 108:2-109:8. There is thus little

reason to believe Natera identified an erroneous inventorship group when it originally filed for the '220, '482, '172, and '841 patents. Certainly, there is little reason to believe that Natera made such gross errors with respect to its inventorship identification.

364. Consistent with this, the testimony of several of the removed inventors establishes that they contributed to the alleged inventions of the '220, '482, '172, and '841 patents.

365. [redacted]

366. [redacted]

367. [redacted]

368. [redacted]

369. [redacted]

370. [redacted]

371. [redacted]

[redacted]

372. [redacted]

373. [redacted]

374. While the evidence shows that the individuals Natera now wishes to remove and has omitted as inventors participated in work directly related to the alleged inventions of the '220, '482, '172, and '841 patents, Natera's efforts to have the inventorship group involved no substantive inquiry into such efforts.

375. [redacted]

[redacted]

376. [redacted]

377. [redacted]

378. [redacted]

379. [redacted]

380. [redacted]

381. [redacted]

382. [redacted]

383. Such testimony underscores the dubiousness of Natera's attempt to change the inventorship groups on the '814, '482, '172, and '220 patents. [redacted]

With respect to all of the foregoing witnesses discussed herein, Natera asserted the attorney-client privilege as to any substantive information regarding inventorship.

384. The testimony-to-date of the inventors establishes that Natera has requested that several inventors withdraw their status as inventors without any basis related to the technical contributions these individuals made to the alleged inventions of the '814, '482, '172, and '220

patents. Rather, Natera's motive in making this request was simply to remove inventors that would jeopardize its ability to improperly claim the benefit of an earlier alleged invention date. This was done with deceptive intent. This deceptive intent and bad faith is shown at least by (1) the testimony from the allegedly improperly included inventors establishing that they contributed to the claimed inventions '814, '482, '172, and '220 patents, (2) the testimony from the allegedly improperly omitted inventor establishing that she did not contribute to the claimed inventions of the '814, '482, '172, and '220 patents, (3), the testimony from the allegedly improperly included and omitted inventors establishing that they signed the documents to change inventorship at the behest of Natera's attorneys without justification and without basis, (4) the testimony from the allegedly improperly included and omitted inventors establishing that Natera did not provide these individuals with any meaningful information in connection with the submission of documents to change inventorship, and (5) Natera's assertion of the privilege to shield discovery of information regarding the submission of documents to change inventorship.

385. Natera's misrepresentation of inventors to the Patent Office was highly material. Title 35 U.S.C. § 115 provides that "An application for patent ... shall include, or be amended to include, the name of the inventor for any invention claimed in the application." Section 115 further states, "Except as otherwise provided in this section, each individual who is the inventor or a joint inventor of a claimed invention in an application for patent shall execute an oath or declaration in connection with the application." The Manual of Patent Examining Procedure ("MPEP") thus instructs examiners to reject applications with improper inventorship. See MPEP § 2137.01 (explaining that "U.S. patent law" requires "naming of the actual inventors"). The MPEP explains that "if a determination is made that the inventive entity named in a U.S. application is not correct . . . a rejection should be made on this basis." *Id.* "As a critical

requirement for obtaining a patent, inventorship is material." *PerSeptive Biosystems, Inc. v. Pharmacia Biotech, Inc.*, 225 F.3d 1315, 1321 (Fed. Cir. 2000).

386. Likewise, Natera's withholding of Defendants' invalidity arguments and the fact that several of the originally named inventors were not even affiliated with Natera until long after Natera's alleged invention date was material.

387. The Examiner responsible for handling the '814, '482, '172, and '220 patents patent appears to have been under the impression that the relevant priority date for the patents in the patent family was this time frame, stating in the notice of allowance for U.S. Patent No. 10,316,362 that the "prior art does not teach a high level of multiplex amplification of more than 1000 targets simultaneously prior to 2011." *See* Ex. 21.

388. Had the Examiner been apprised of the fact that Natera's original inventorship group included individuals that were not even affiliated with Natera until long after this time frame and that Natera was seeking to remove such individuals as inventors from certain patents and add other inventors to other patents, the Examiner would have more thoroughly questioned and likely rejected Natera's priority claim and would have identified substantial prior art that invalidates the '814, '482, '172, and '220 patents. As such, Natera's misrepresentations and withholding of information was material and the '814, '482, '172, and '220 patents are unenforceable due to inequitable conduct.

ARCHERDX'S COUNTERCLAIMS

Defendants/Counterclaimants Invitae Corp. ("Invitae") and ArcherDX, LLC ("ArcherDX") (together, "the Counterclaimants") assert Counterclaims against Plaintiff/Counterclaim-Defendant Natera, Inc. ("Natera") as follows:

NATURE OF ACTION

1. For its Counterclaims, the Counterclaimants seek declarations that its LIQUIDPlex™, FusionPlex® and VariantPlex® products do not infringe U.S. Patent Nos. 10,538,814 ("the '814 Patent"), 10,557,172 ("the '172 Patent"), 10,590,482 ("the '482 Patent"), 10,597,708 ("the '708 Patent"), and 10,731,220 ("the '220 Patent") (collectively, the "Asserted Patents") and that the Asserted Patents are invalid.

PARTIES

2. ArcherDX, LLC is a limited liability company, organized and existing under the laws of the State of Delaware. ArcherDX, Inc. was, at the time of the filing of the action, a Delaware corporation with a principal place of business at 2477 55th Street, Suite 202, Boulder, Colorado 80301.

3. Invitae is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 1400 16th Street, San Francisco, CA 94103. On information and belief, and as alleged by Natera in its Second Amended Complaint, Natera is a corporation organized and existing under the laws of the state of Delaware, with its principal place of business at 201 Industrial Road, San Carlos, California 94070.

JURISDICTION AND VENUE

4. This Court has subject matter jurisdiction over this action under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202 as to ArcherDX's counterclaims against Natera pursuant to the patent laws of the United States, Title 35, United States Code, and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. An actual, substantial, and continuing justiciable controversy exists between Natera and the Counterclaimants based on Natera having filed a Second Amended Complaint against the Counterclaimants alleging infringement of the Asserted Patents by sales of LIQUIDPlex™, FusionPlex® and VariantPlex®, for research use only, with respect to which

Counterclaimants require declaration of its rights by this Court. Specifically, the controversy concerns non- infringement and invalidity of the Asserted Patents.

5. Personal jurisdiction over Natera is proper because Natera has submitted itself to the jurisdiction of this Court by, among other things, filing the Second Amended Complaint.

6. To the extent venue is proper in the underlying patent infringement action, venue is proper here as to these Counterclaims under 28 U.S.C. §§ 1391(b)–(c) and 28 U.S.C. § 1400(b).

FIRST COUNTERCLAIM
(Declaratory Judgment of Non-Infringement of the '814 Patent)

7. The Counterclaimants reallege and incorporates its preliminary statement, and the allegations set forth in paragraphs 1-6 of these Counterclaims as if fully restated herein.

8. In its Second Amended Complaint, Natera alleges that the Counterclaimants infringed and continue to infringe the '814 Patent by its sale of LIQUIDPlex™, FusionPlex®, and VariantPlex® for research use only.

9. The Counterclaimants have not and are not now infringing, inducing the infringement of, or contributing to the infringement of any valid and enforceable claim of the '814 Patent by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

10. For example, claim 1 of the '814 Patent recites "performing a first PCR...using a universal primer" and "performing a second, nested PCR...using the universal primer and at least 10 inner target-specific primers..., wherein at least one of the primers comprises a sequencing tag." ArcherDX's LIQUIDPlex™ , FusionPlex®, and VariantPlex® products do not employ "a second, nested PCR... using the universal primer" of the first PCR, nor do the products employ

"at least one of the primers comprises a sequencing tag."

11. The Counterclaimants further lacked and continue to lack the requisite intent or knowledge to induce or contribute to the direct infringement of the '814 Patent by another by its sale of LIQUIDPlex™, FusionPlex®, and VariantPlex® for research use only.

12. A justiciable controversy exists as to whether the Counterclaimants have infringed any valid and enforceable claim of the '814 Patent by its sale of LIQUIDPlex™, FusionPlex®, and VariantPlex® for research use only.

13. The Counterclaimants are entitled to a judgment declaring that the Counterclaimants have not directly or indirectly infringed, either literally or under the doctrine of equivalents, any valid and enforceable claim of the '814 Patent by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

SECOND COUNTERCLAIM
(Declaratory Judgment of Invalidity of the '814 Patent)

14. The Counterclaimants reallege and incorporate its preliminary statement, and the allegations set forth in paragraphs 1-13 of these Counterclaims as if fully restated herein.

15. The claims of the '814 Patent are invalid in view of the prior art and/or for failure to comply with one or more conditions for patentability set forth under 35 U.S.C. including but not limited to §§ 101, 102, 103, and 112 et seq., and the rules, regulations, and laws pertaining to those provisions, including the applicable provisions of Title 37 of the Code of Federal Regulations.

16. The Counterclaimants are entitled to judgment declaring that the claims of the '814 Patent are invalid in view of the prior art and/or for failure to comply with one or more of the

requirements of the United States Patent Act set out in 35 U.S.C. §§ 1, et seq., including without limitation 35 U.S.C. §§ 101, 102, 103, and 112.

Invalidity under 35 U.S.C. § 101

17. Accepting as true Natera's own statements made in proceedings in this District and elsewhere, the claims of the '814 Patent are directed to unpatentable naturally occurring subject matter, phenomena, and/or relationships, and any additional elements in the claims are merely well-understood, routine, or conventional. Thus, the claims of the '814 Patent are unpatentable under 35 U.S.C. § 101.

18. For example, in another case pending in this District, *CareDX, Inc. et al. v. Natera, Inc.*, No. 19-cv-567 (D. Del.) ("CareDX"), Natera has alleged that the claims of the two patents-in-suit there—U.S. Patent Nos. 8,703,652 and 9,845,497—are unpatentable under 35 U.S.C. § 101. *See CareDX*, No. 19-cv-567, D.I. 9-10, 19 (Natera's Motion to Dismiss and Briefing Related Thereto), 63 (Natera's Objections to Report and Recommendation) (attached as Exhibits 1-4); *see also id.*, D.I. 86, 87 (Natera's Renewed Motion to Dismiss) (attached as Exhibits 7-8). The two patents asserted in CareDX claim priority to applications filed in 2009 and 2010, which is before the earliest possible priority date for the claims of the '814 Patent.

19. Similarly, in *Illumina, Inc. v. Natera, Inc.*, No. 18-cv-01662 (N.D. Cal.) ("Illumina"), Natera has alleged that the claims of U.S. Patent No. 9,493,831 are unpatentable under Section 101. *See Illumina*, No. 18-cv-01662, D.I. 24, 35 (Motion to Dismiss and Briefing Related Thereto) (attached as Exhibits 5-6). The patent asserted in Illumina claims priority to an application filed in 2010, which is before the earliest possible priority date for the claims of the '814 Patent.

20. In this case, representative claim 1 of the '814 Patent recites a "a method for amplifying and sequencing DNA" comprising (1) ligating adaptors to isolated cell-free DNA, (2) performing a first round of polymerase chain reaction (PCR), (3) performing a second, "nested"

round of PCR that includes use of a sequencing tag, and (4) performing high-throughput sequencing to sequence the cell-free DNA.

21. But in *CareDX*, Natera itself acknowledged that cell-free DNA is a natural phenomenon, and alleged that amplification and sequencing methods, such as PCR and high throughput sequencing, were known and used in the art to detect and sequence cell-free DNA. *E.g., CareDX*, D.I. 10 at 12-19; D.I. 19 at 6-7; D.I. 63 at 3-5. And in Illumina, Natera also argued that cell-free DNA is "naturally occurring," and the use of "well-known, routine, and conventional amplification techniques"—including nested PCR, and the use of primers with attached sequencing tags—to amplify and sequence the DNA is not patentable. *See Illumina*, No. 18-cv-01662, D.I. 24 at 2, 6-8; D.I. 35 at 2-9.

22. Thus, by Natera's own admissions, the claims of the '814 Patent are unpatentable under 35 U.S.C. § 101, and Natera should never have filed its Second Amended Complaint against the Counterclaimants.

Invalidity under 35 U.S.C. §§ 102 and 103

23. The claims of the '814 Patent are invalid under 35 U.S.C. § 102 and/or § 103, in view of, for example, the following prior art, alone or in combination with additional prior art: Mir, with Wang, Spertini, or Makarov, which disclose all elements of the '814 Patent claims. Natera disclosed Mir as one of *thousands* of references during prosecution of the '814 Patent. Natera did not disclose either Wang, Spertini, or Makarov to the USPTO during prosecution of the '814 Patent. Moreover, the '814 Patent is at least obvious under 35 U.S.C. § 103 given Natera's own admissions made in court filings in this District and elsewhere, representative examples of which are set forth above in paragraphs 17-22.

24. The ’814 Patent is also not entitled to a priority date earlier than its filing date of April 30, 2019, because Natera’s provisional applications and earlier-filed applications do not

comply with the requirements of 35 U.S.C § 112, as required by 35 U.S.C §§ 119 and 120. The provisional applications and earlier-filed applications do not contain a written description of the claims of the '814 Patent or contain sufficient information to enable a person of ordinary skill in the art to which they pertain to practice the full scope of the claims of the '814 Patent. Indeed, none of the provisional applications or earlier-filed applications disclosed or sought claims corresponding to the claims of the '814 Patent, which recite processes that Natera did not invent.

25. Because the '814 Patent is not entitled to a priority date earlier than its filing date of April 30, 2019, it is invalid under 35 U.S.C. § 102 and/or § 103, in further view of, for example, the following prior art, alone or in combination with additional prior art: Hu or Murtaza, which disclose all elements of the '814 Patent claims. Natera did not disclose either Hu or Murtaza to the USPTO during prosecution of the '814 Patent. Moreover, the '814 Patent is at least obvious under 35 U.S.C. § 103 given Natera's own admissions made in court filings in this District and elsewhere, representative examples of which are set forth above in paragraphs 17-~~-~~22.

26. The '814 patent is further invalid for failing to name the proper inventors under 35 U.S.C. § 102(f), as set forth above in paragraphs 354-88 of Defendants' answer.

Invalidity under 35 U.S.C. § 112 and Improper Inventorship

~~26~~27. The claims of the '814 Patent are invalid under 35 U.S.C. § 112.

~~27~~28. The claims of the '814 Patent lack written description support in the specification.

~~28~~29. As an example, the specification of the '814 Patent does not disclose an embodiment or example corresponding to claim 1 of the '814 Patent and does not otherwise disclose that the named inventors of the '814 Patent were in possession of the alleged invention recited in the claims as of the priority date of the '814 Patent.

~~29~~30. Indeed, prior to the filing of the '814 Patent application on April 30, 2019, Natera had never disclosed nor sought claims corresponding to the claims of the '814 Patent.

~~30~~31. The specification also does not contain sufficient information to enable a person of

ordinary skill in the art to which the patent pertains to practice the full scope of the claims of the ’814 Patent.

~~31~~32. The ’814 Patent does not satisfy the requirements of 35 U.S.C. § 112 because the

applicants for the ’814 Patent did not themselves invent the subject matter sought to be patented—an independent ground for invalidating the patent.

THIRD COUNTERCLAIM
(Declaratory Judgment of Unenforceability Of The ’814 Patent Due to Inequitable Conduct)

33. The Counterclaimants reallege and incorporate its preliminary statement, and the

allegations set forth in paragraphs 1-31 of these Counterclaims as if fully restated herein.

34. Defendants incorporate herein by reference the facts set forth with particularly in

paragraphs 354-88 of Defendants’ answer above. As alleged in the incorporated paragraphs, the ’814 patent is unenforceable due to inequitable conduct.

FOURTH COUNTERCLAIM
(Declaratory Judgment of Non-Infringement of the ’172 Patent)

~~32~~35. The Counterclaimants reallege and incorporate its preliminary statement, and the

allegations set forth in paragraphs 1-~~31~~34 of these Counterclaims as if fully restated herein.

~~33~~36. In its Second Amended Complaint, Natera alleges that the Counterclaimants have

infringed and continue to infringe the ’172 Patent by its sale of LIQUIDPlex™, FusionPlex®, and VariantPlex® for research use only.

~~34~~37. The Counterclaimants have not and are not now infringing, inducing the

infringement of, or contributing to the infringement of any valid and enforceable claim of the '172 Patent by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

~~35~~38. For example, claim 1 of the '172 Patent recites "performing a first PCR...using a

universal primer" and "performing a second, nested PCR...using the universal primer." ArcherDX's LIQUIDPlex™, FusionPlex®, and VariantPlex® products do not include "a second, nested PCR... using the universal primer" of the first PCR.

3639. The Counterclaimants further lacked and continue to lack the requisite intent or knowledge to induce or contribute to the direct infringement of the '172 Patent by another by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

3740. A justiciable controversy exists as to whether the Counterclaimants have infringed any valid and enforceable claim of the '172 Patent by its sale of LIQUIDPlex™, FusionPlex®, and VariantPlex® for research use only.

3841. The Counterclaimants are entitled to a judgment declaring that the Counterclaimants have not directly or indirectly infringed, either literally or under the doctrine of equivalents, any valid and enforceable claim of the '172 Patent by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

FOURTHFIFTH COUNTERCLAIM
(Declaratory Judgment of Invalidity of the '172 Patent)

3942. The Counterclaimants reallege and incorporate its preliminary statement, and the allegations set forth in paragraphs 1-3841 of these Counterclaims as if fully restated herein.

4043. The claims of the '172 Patent are invalid in view of the prior art and/or for failure to comply with one or more conditions for patentability set forth under 35 U.S.C. including but not limited to §§ 101, 102, 103, and 112 et seq., and the rules, regulations, and laws pertaining to those provisions, including the applicable provisions of Title 37 of the Code of Federal Regulations.

~~41~~44. The Counterclaimants are entitled to judgment declaring that the claims of the '172 Patent are invalid in view of the prior art and/or for failure to comply with one or more of the requirements of the United States Patent Act set out in 35 U.S.C. §§ 1, et seq., including without limitation 35 U.S.C. §§ 101, 102, 103, and 112.

Invalidity under 35 U.S.C. § 101

~~42~~45. Accepting as true Natera's own statements made in proceedings in this District and elsewhere, the claims of the '172 Patent are directed to unpatentable naturally occurring subject matter, phenomena, and/or relationships, and any additional elements in the claims are merely well-understood, routine, or conventional. Thus, the claims of the '172 Patent are unpatentable under 35 U.S.C. § 101.

~~43~~46. For example, in CareDX, Natera has alleged that the claims of the two patents-in-suit there—U.S. Patent Nos. 8,703,652 and 9,845,497—are unpatentable under 35 U.S.C. § 101. *See* Exs. 1-4, 7-8. The two patents asserted in CareDX claim priority to applications filed in 2009 and 2010, which is before the earliest possible priority date for the claims of the '172 Patent.

~~44~~47. Similarly, in Illumina, Natera has alleged that the claims of U.S. Patent No. 9,493,831 are unpatentable under Section 101. *See* Exs. 5-6. The patent asserted in Illumina claims priority to an application filed in 2010, which is before the earliest possible priority date for the claims of the '172 Patent.

~~45~~48. In this case, representative claim 1 of the '172 Patent recites a "a method for amplifying and sequencing DNA" comprising (1) isolating and tagging cell-free DNA with a molecular barcode, (2) performing a first round of polymerase chain reaction (PCR), (3) performing a second, "nested" round of PCR, and (4) performing high-throughput sequencing to sequence the cell-free DNA.

~~46~~49. But in CareDX, Natera itself acknowledged that cell-free DNA is a natural phenomenon, and alleged that amplification and sequencing methods, such as PCR and high throughput sequencing, were known and used in the art to detect and sequence cell-free DNA. *E.g., CareDX*, D.I. 10 at 12-19; D.I. 19 at 6-7; D.I. 63 at 3-5. And in Illumina, Natera also argued

that cell-free DNA is "naturally occurring," and the use of "well-known, routine, and conventional amplification techniques"—including nested PCR, and the use of primers—to amplify and sequence the DNA is not patentable. *See Illumina,* No. 18-cv-01662, D.I. 24 at 2, 6-8; D.I. 35 at 29.

47~~50~~. Thus, by Natera's own admissions, the claims of the '172 Patent are unpatentable under 35 U.S.C. § 101, and Natera should never have filed its Second Amended Complaint against the Counterclaimants.

Invalidity under 35 U.S.C. §§ 102 and 103

48~~51~~. The claims of the '172 Patent are invalid under 35 U.S.C. § 102 and/or § 103, in view of, for example, the following prior art, alone or in combination with additional prior art: Mir, with Wang, Spertini, or Makarov, which disclose all elements of the '172 Patent claims. Natera disclosed Mir as one of *thousands* of references during prosecution of the '172 Patent. Natera did not disclose either Wang, Spertini, or Makarov to the USPTO during prosecution of the '172 Patent. Moreover, the '172 Patent is at least obvious under 35 U.S.C. § 103 given Natera's own admissions made in court filings in this District and elsewhere, representative examples of which are set forth above in paragraphs 42~~45~~-47~~50~~.

49~~52~~. The '172 Patent is also not entitled to a priority date earlier than its filing date of April 30, 2019, because Natera's provisional applications and earlier-filed applications do not comply with the requirements of 35 U.S.C § 112, as required by 35 U.S.C §§ 119 and 120. The provisional applications and earlier-filed applications do not contain a written description of the

claims of the '172 Patent or contain sufficient information to enable a person of ordinary skill in the art to which they pertain to practice the full scope of the claims of the '172 Patent. Indeed,

none of the provisional applications or earlier-filed applications disclosed or sought claims corresponding to the claims of the '172 Patent, which recite processes that Natera did not invent.

~~50~~53. Because the '172 Patent is not entitled to a priority date earlier than its filing date of April 30, 2019, it is invalid under 35 U.S.C. § 102 and/or § 103, in further view of, for example, the following prior art, alone or in combination with additional prior art: Hu or Murtaza, which disclose all elements of the '172 Patent claims. Natera did not disclose either Hu or Murtaza to the USPTO during prosecution of the '172 Patent. Moreover, the '172 Patent is at least obvious under 35 U.S.C. § 103 given Natera's own admissions made in court filings in this District and elsewhere, representative examples of which are set forth above in paragraphs ~~42~~45-~~47~~50.

54. The '172 patent is further invalid for failing to name the proper inventors under 35 U.S.C. § 102(f), as set forth above in paragraphs 354-88 of Defendants' answer.

Invalidity under 35 U.S.C. § 112 and Improper Inventorship

~~51~~55. The claims of the '172 Patent are invalid under 35 U.S.C. § 112.

~~52~~56. The claims of the '172 Patent lack written description support in the specification.

~~53~~57. As an example, the specification of the '172 Patent does not disclose an embodiment or example corresponding to claim 1 of the '172 Patent and does not otherwise disclose that the named inventors of the '172 Patent were in possession of the alleged invention recited in the claims as of the priority date of the '172 Patent.

~~54~~58. Indeed, prior to the filing of the '172 Patent application on April 30, 2019, Natera had never disclosed nor sought claims corresponding to the claims of the '172 Patent.

~~55~~59. The specification also does not contain sufficient information to enable a person of

ordinary skill in the art to which the patent pertains to practice the full scope of the claims of the '172 Patent.

5660. The '172 Patent does not satisfy the requirements of 35 U.S.C. § 112 because the applicants for the '172 Patent did not themselves invent the subject matter sought to be patented—an independent ground for invalidating the patent.

FIFTHSIXTH COUNTERCLAIM
(Declaratory Judgment of Unenforceability Of The '172 Patent Due to Inequitable Conduct)

61. The Counterclaimants reallege and incorporate its preliminary statement, and the allegations set forth in paragraphs 1-60 of these Counterclaims as if fully restated herein.

62. Defendants incorporate herein by reference the facts set forth with particularly in paragraphs 354-88 of their answer above. As alleged in the incorporated paragraphs, the '172 patent is unenforceable due to inequitable conduct.

SEVENTH COUNTERCLAIM
(Declaratory Judgment of Non-Infringement of the '482 Patent)

5763. The Counterclaimants reallege and incorporate its preliminary statement, and the allegations set forth in paragraphs 1-5662 of these Counterclaims as if fully restated herein.

5864. In its Second Amended Complaint, Natera alleges that the Counterclaimants have infringed and continue to infringe the '482 Patent by its sale of LIQUIDPlex™, FusionPlex®, and VariantPlex® for research use only.

5965. The Counterclaimants have not and are not now infringing, inducing the infringement of, or contributing to the infringement of any valid and enforceable claim of the '482 Patent by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

~~60~~66. For example, claim 1 of the '482 Patent recites "performing a first PCR...using a

universal primer" and "performing a second, nested PCR...using the universal primer." ArcherDX's LIQUIDPlex™ , FusionPlex®, and VariantPlex® products do not employ "a second, nested PCR...using the universal primer" of the first PCR.

~~61~~67. The Counterclaimants further lacked and continue to lack the requisite intent or

knowledge to induce or contribute to the direct infringement of the '482 Patent by another by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

~~62~~68. A justiciable controversy exists as to whether the Counterclaimants have infringed

any valid and enforceable claim of the '482 Patent by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

~~63~~69. The Counterclaimants are entitled to a judgment declaring that the

Counterclaimants have not directly or indirectly infringed, either literally or under the doctrine of equivalents, any valid and enforceable claim of the '482 Patent by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

~~SIXTH~~EIGHTH COUNTERCLAIM
(Declaratory Judgment of Invalidity of the '482 Patent)

~~64~~70. The Counterclaimants reallege and incorporate its preliminary statement, and the

allegations set forth in paragraphs 1-~~63~~69 of these Counterclaims as if fully restated herein.

~~65~~71. The claims of the '482 Patent are invalid in view of the prior art and/or for failure

to comply with one or more conditions for patentability set forth under 35 U.S.C. including but not limited to §§ 101, 102, 103, and 112 et seq., and the rules, regulations, and laws pertaining to

those provisions, including the applicable provisions of Title 37 of the Code of Federal Regulations.

~~66~~72. The Counterclaimants are entitled to judgment declaring that the claims of the '482 Patent are invalid in view of the prior art and/or for failure to comply with one or more of the requirements of the United States Patent Act set out in 35 U.S.C. §§ 1, et seq., including without limitation 35 U.S.C. §§ 101, 102, 103, and 112.

Invalidity under 35 U.S.C. § 101

~~67~~73. Accepting as true Natera's own statements made in proceedings in this District and elsewhere, the claims of the '482 Patent are directed to unpatentable naturally occurring subject matter, phenomena, and/or relationships, and any additional elements in the claims are merely well-understood, routine, or conventional. Thus, the claims of the '482 Patent are unpatentable under 35 U.S.C. § 101.

~~68~~74. For example, in CareDX, Natera has alleged that the claims of the two patents-in-suit there—U.S. Patent Nos. 8,703,652 and 9,845,497—are unpatentable under 35 U.S.C. § 101. *See* Exs. 1-4, 7-8. The two patents asserted in CareDX claim priority to applications filed in 2009 and 2010, which is before the earliest possible priority date for the claims of the '482 Patent.

~~69~~75. Similarly, in Illumina, Natera has alleged that the claims of U.S. Patent No. 9,493,831 are unpatentable under Section 101. *See* Exs. 5-6. The patent asserted in Illumina claims priority to an application filed in 2010, which is before the earliest possible priority date for the claims of the '482 Patent.

~~70~~76. In this case, representative claim 1 of the '482 Patent recites a "a method for nested PCR amplification" comprising (1) isolating cell-free DNA; (2) ligating adaptors to isolated cell-free DNA, (3) performing a first round of polymerase chain reaction (PCR), and (4) performing a second, "nested" round of PCR.

~~71~~77. But in CareDX, Natera itself acknowledged that cell-free DNA is a natural

phenomenon, and alleged that amplification methods, such as PCR, were known and used in the

art to detect cell-free DNA. *E.g.*, CareDX, D.I. 10 at 12-19; D.I. 19 at 6-7; D.I. 63 at 3-5. And in Illumina, Natera also argued that cell-free DNA is "naturally occurring," and the use of "well-known, routine, and conventional amplification techniques"—including nested PCR—to amplify and sequence the DNA is not patentable. *See Illumina*, No. 18-cv-01662, D.I. 24 at 2, 6-8; D.I. 35 at 2-9.

~~72~~78. Thus, by Natera's own admissions, the claims of the '482 Patent are unpatentable under 35 U.S.C. § 101, and Natera should never have filed its Second Amended Complaint against the Counterclaimants.

Invalidity under 35 U.S.C. §§ 102 and 103

~~73~~79. The claims of the '482 Patent are invalid under 35 U.S.C. § 102 and/or § 103, in view of, for example, the following prior art, alone or in combination with additional prior art: Mir, with Wang, Spertini, or Makarov, which disclose all elements of the '482 Patent claims. Natera disclosed Mir as one of *thousands* of references during prosecution of the '482 Patent. Natera did not disclose either Wang, Spertini, or Makarov to the USPTO during prosecution of the '482 Patent. Moreover, the '482 Patent is at least obvious under 35 U.S.C. § 103 given Natera's own admissions made in court filings in this District and elsewhere, representative examples of which are set forth above in paragraphs ~~67~~73-~~72~~78.

~~74~~80. The '482 Patent is also not entitled to a priority date earlier than its filing date of April 30, 2019, because Natera's provisional applications and earlier-filed applications do not comply with the requirements of 35 U.S.C § 112, as required by 35 U.S.C §§ 119 and 120. The provisional applications and earlier-filed applications do not contain a written description of the claims of the '482 Patent or contain sufficient information to enable a person of ordinary skill in the art to which they pertain to practice the full scope of the claims of the '482 Patent. Indeed,

none of the provisional applications or earlier-filed applications disclosed or sought claims corresponding to the claims of the '482 Patent, which recite processes that Natera did not invent.

~~75~~81. Because the '482 Patent is not entitled to a priority date earlier than its filing date of April 30, 2019, it is invalid under 35 U.S.C. § 102 and/or § 103, in further view of, for example, the following prior art, alone or in combination with additional prior art: Hu or Murtaza, which

disclose all elements of the ’482 Patent claims. Natera did not disclose either Hu or Murtaza to the USPTO during prosecution of the ’482 Patent. Moreover, the ’482 Patent is at least obvious under 35 U.S.C. § 103 given Natera’s own admissions made in court filings in this District and elsewhere, representative examples of which are set forth above in paragraphs ~~67~~73-~~72~~78.

82. The ’482 patent is further invalid for failing to name the proper inventors under 35 U.S.C. § 102(f), as set forth above in paragraphs 354-88 of Defendants’ answer.

Invalidity under 35 U.S.C. § 112 and Improper Inventorship

~~76~~83. The claims of the ’482 Patent are invalid under 35 U.S.C. § 112.

~~77~~84. The claims of the ’482 Patent lack written description support in the specification.

~~78~~85. As an example, the specification of the ’482 Patent does not disclose an embodiment or example corresponding to claim 1 of the ’482 Patent and does not otherwise disclose that the named inventors of the ’482 Patent were in possession of the alleged invention recited in the claims as of the priority date of the ’482 Patent.

~~79~~86. Indeed, prior to the filing of the ’482 Patent application on April 30, 2019, Natera had never disclosed nor sought claims corresponding to the claims of the ’482 Patent.

~~80~~87. The specification also does not contain sufficient information to enable a person of ordinary skill in the art to which the patent pertains to practice the full scope of the claims of the ’482 Patent.

~~81~~88. The ’482 Patent does not satisfy the requirements of 35 U.S.C. § 112 because the

applicants for the ’482 Patent did not themselves invent the subject matter sought to be patented—an independent ground for invalidating the patent.

~~SEVENTH~~NINTH COUNTERCLAIM
(Declaratory Judgment of Unenforceability Of The '482 Patent Due to Inequitable Conduct)

89. The Counterclaimants reallege and incorporate its preliminary statement, and the allegations set forth in paragraphs 1-85 of these Counterclaims as if fully restated herein.

90. Defendants incorporate herein by reference the facts set forth with particularly in paragraphs 354-88 of their answer above. As alleged in the incorporated paragraphs, the '482 patent is unenforceable due to inequitable conduct.

TENTH COUNTERCLAIM
(Declaratory Judgment of Non-Infringement of the '708 Patent)

~~82~~91. The Counterclaimants reallege and incorporate its preliminary statement, and the allegations set forth in paragraphs 1-~~81~~90 of these Counterclaims as if fully restated herein.

~~83~~92. In its Second Amended Complaint, Natera alleges that ArcherDX has infringed and continues to infringe the '708 Patent by its sale of LIQUIDPlex™, FusionPlex®, and VariantPlex® for research use only.

~~84~~93. The Counterclaimants have not and are not now infringing, inducing the infringement of, or contributing to the infringement of any valid and enforceable claim of the '708 Patent by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

~~85~~94. For example, claim 1 of the '708 Patent recites "subjecting the reaction mixture to primer extension reaction conditions...; wherein annealing temperature for the reaction conditions is greater than a melting temperature of the at least 2 primers." ArcherDX's LIQUIDPlex™ , FusionPlex®, and VariantPlex® products do not employ reaction conditions "wherein the annealing

temperature for the reaction conditions is greater than a melting temperature of the at least 2 primers."

~~86~~95. The Counterclaimants further lacked and continue to lack the requisite intent or knowledge to induce or contribute to the direct infringement of the '708 Patent by another by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

~~87~~96. A justiciable controversy exists as to whether the Counterclaimants have infringed any valid and enforceable claim of the '708 Patent by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

~~88~~97. The Counterclaimants are entitled to a judgment declaring that the Counterclaimants have not directly or indirectly infringed, either literally or under the doctrine of

equivalents, any valid and enforceable claim of the '708 Patent by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only.

~~EIGHTH~~ELEVENTH COUNTERCLAIM
(Declaratory Judgment of Invalidity of the '708 Patent)

98~~9~~. The Counterclaimants reallege and incorporate its preliminary statement, and the allegations set forth in paragraphs 1-~~88~~97 of these Counterclaims as if fully restated herein.

~~90~~99. The claims of the '708 Patent are invalid in view of the prior art and/or for failure to comply with one or more conditions for patentability set forth under 35 U.S.C. including but not limited to §§ 101, 102, 103, and 112 et seq., and the rules, regulations, and laws pertaining to those provisions, including the applicable provisions of Title 37 of the Code of Federal Regulations.

~~91~~100. The Counterclaimants are entitled to judgment declaring that the claims of the '708 Patent are invalid in view of the prior art and/or for failure to comply with one or more of the

requirements of the United States Patent Act set out in 35 U.S.C. §§ 1, et seq., including without limitation 35 U.S.C. §§ 101, 102, 103, and 112.

Invalidity under 35 U.S.C. § 101

~~92~~101. Accepting as true Natera's own statements made in proceedings in this District and elsewhere, the claims of the '708 Patent are directed to unpatentable naturally occurring subject matter, phenomena, and/or relationships, and any additional elements in the claims are merely well-understood, routine, or conventional. Thus, the claims of the '708 Patent are unpatentable under 35 U.S.C. § 101.

~~93~~102. For example, in *CareDX*, Natera has alleged that the claims of the two patents-in-suit there—U.S. Patent Nos. 8,703,652 and 9,845,497—are unpatentable under 35 U.S.C. § 101. *See* Exs. 1-4, 7-8. The two patents asserted in CareDX claim priority to applications filed in 2009 and 2010, which is before the earliest possible priority date for the claims of the '708 Patent.

~~94~~103. Similarly, in *Illumina*, Natera has alleged that the claims of U.S. Patent No. 9,493,831 are unpatentable under Section 101. *See* Exs. 5-6. The patent asserted in Illumina claims priority to an application filed in 2010, which is before the earliest possible priority date for the claims of the '708 Patent.

~~95~~104. In this case, representative claim 1 of the '708 Patent recites "a method for amplifying target loci in a nucleic acid sample" comprising (1) contacting a nucleic acid with target-specific primers, and (2) subjecting the reaction mixture to amplification reaction conditions.

~~96~~105. But in CareDX, Natera itself acknowledged that nucleic acids are a natural phenomenon, and alleged that amplification methods were known and used in the art to detect nucleic acids. E.g., CareDX, D.I. 10 at 12-19; D.I. 19 at 6-7; D.I. 63 at 3-5. And in Illumina, Natera also argued that nucleic acids are "naturally occurring," and the use of "well- known, routine, and

conventional amplification techniques"—including the use of primers—to amplify the nucleic acid is not patentable. *See Illumina*, No. 18-cv-01662, D.I. 24 at 2, 6-8; D.I. 35 at 2-9.

~~97~~106. Thus, by Natera's own admissions, the claims of the '708 Patent are unpatentable under 35 U.S.C. § 101, and Natera should never have filed its Second Amended Complaint against the Counterclaimants.

Invalidity under 35 U.S.C. §§ 102 and 103

98107. The claims of the '708 Patent are invalid under 35 U.S.C. § 102 and/or § 103, in view of, for example, the following prior art, alone or in combination with additional prior art: Iafrate and Rabinowitz, which disclose all elements of the '708 Patent claims. Natera disclosed a related Iafrate application (U.S. Patent App. Pub. No. 2013/0303461) and Rabinowitz as two of *thousands* of references during prosecution of the '708 Patent. Moreover, the '708 Patent is at least obvious under 35 U.S.C. § 103 given Natera's own admissions made in court filings in this District and elsewhere, representative examples of which are set forth above in paragraphs 92101- 9706.

99108. The '708 Patent is also not entitled to a priority date earlier than its filing date of April 30, 2019, because Natera's provisional applications and earlier-filed applications do not comply with the requirements of 35 U.S.C § 112, as required by 35 U.S.C §§ 119 and 120. The provisional applications and earlier-filed applications do not contain a written description of the claims of the '708 Patent or contain sufficient information to enable a person of ordinary skill in the art to which they pertain to practice the full scope of the claims of the '708 Patent. Indeed, none of the provisional applications or earlier-filed applications disclosed or sought claims corresponding to the claims of the '708 Patent, which recite processes that Natera did not invent.

Invalidity under 35 U.S.C. § 112 and Improper Inventorship

1009. The claims of the '708 Patent are invalid under 35 U.S.C. § 112.

~~101~~110. The claims of the '708 Patent lack written description support in the specification

and are indefinite.

~~102~~111. As an example, the specification of the '708 Patent does not disclose an

embodiment or example corresponding to claim 1 of the '708 Patent and does not otherwise

disclose that the named inventors of the '708 Patent were in possession of the alleged invention recited in the claims as of the priority date of the '708 Patent.

~~103~~112. Indeed, prior to the filing of the '708 Patent application on April 30, 2019, Natera had never disclosed nor sought claims corresponding to the claims of the '708 Patent.

~~104~~113. The specification also does not contain sufficient information to enable a person of ordinary skill in the art to which the patent pertains to practice the full scope of the claims of the '708 Patent.

~~105~~114. Moreover, the claims of the '708 Patent are indefinite because the claim language, read in light of the specification and prosecution history, fails to inform, with reasonable certainty, those skilled in the art about the scope of the alleged invention.

~~106~~115. The '708 Patent does not satisfy the requirements of 35 U.S.C. § 112 because the applicants for the '708 Patent did not themselves invent the subject matter sought to be patented—an independent ground for invalidating the patent.

~~NINTH~~TWELFTH COUNTERCLAIM
(Declaratory Judgment of Non-Infringement of the '220 Patent)

~~107~~116. The Counterclaimants reallege and incorporate its preliminary statement, and the allegations set forth in paragraphs 1-~~106~~115 of these Counterclaims as if fully restated herein.

~~108~~117. In its Complaint, Natera alleges that the Counterclaimants have infringed and continue to infringe the '220 Patent by its sale of LIQUIDPlex™ or VariantPlex® for research use only.

~~109~~118. The Counterclaimants have not and is not now infringing, inducing the

infringement of, or contributing to the infringement of any valid and enforceable claim of the '220 Patent by its sale of LIQUIDPlex™ or VariantPlex® for research use only.

1109. For example, claim 1 of the ’220 Patent recites “performing a second, nested PCR...using a second universal primer and at least 10 inner target-specific primers..., wherein at least one of the primers comprises a sequencing tag.” ArcherDX’s accused AMP™ process does not include “a second, nested PCR...wherein at least one of the [second universal primer and at least 10 inner target-specific primers] comprises a sequencing tag.”

111120. The Counterclaimants further lacked and continue to lack the requisite intent or knowledge to induce or contribute to the direct infringement of the ’220 Patent by another by its sale of LIQUIDPlex™ or VariantPlex® for research use only.

112121. A justiciable controversy exists as to whether the Counterclaimants have infringed any valid and enforceable claim of the ’220 Patent by its sale of LIQUIDPlex™ and VariantPlex® for research use only.

113122. The Counterclaimants are entitled to a judgment declaring that the Counterclaimants have not directly or indirectly infringed, either literally or under the doctrine of equivalents, any valid and enforceable claim of the ’220 Patent by its sale of LIQUIDPlex™ or VariantPlex® for research use only.

TENTHTHIRTEENTH COUNTERCLAIM
(Declaratory Judgment of Invalidity of the ’220 Patent)

114123. The Counterclaimants reallege and incorporate its preliminary statement, and the allegations set forth in paragraphs 1-113122 of these Counterclaims as if fully restated herein.

115124. The claims of the ’220 Patent are invalid in view of the prior art and/or for failure to comply with one or more conditions for patentability set forth under 35 U.S.C. including but

not limited to §§ 101, 102, 103, and 112 et seq., and the rules, regulations, and laws pertaining to those provisions, including the applicable provisions of Title 37 of the Code of Federal Regulations.

~~116~~125. The Counterclaimants are entitled to judgment declaring that the claims of the '220 Patent are invalid in view of the prior art and/or for failure to comply with one or more of the requirements of the United States Patent Act set out in 35 U.S.C. §§ 1, et seq., including without limitation 35 U.S.C. §§ 101, 102, 103, and 112.

Invalidity under 35 U.S.C. § 101

~~117~~126. Accepting as true Natera's own statements made in proceedings in this District and elsewhere, the claims of the '220 Patent are directed to unpatentable naturally occurring subject matter, phenomena, and/or relationships, and any additional elements in the claims are merely well-understood, routine, or conventional. Thus, the claims of the '220 Patent are unpatentable under 35 U.S.C. § 101.

~~118~~127. For example, in another case pending in this District, *CareDX, Inc. et al. v. Natera, Inc.*, No. 19-cv-567 (D. Del.) ("CareDX"), Natera has alleged that the claims of the two patents-in-suit there—U.S. Patent Nos. 8,703,652 and 9,845,497—are unpatentable under 35 U.S.C. § 101. *See CareDX*, No. 19-cv-567, D.I. 9-10, 19 (Natera's Motion to Dismiss and Briefing Related Thereto), 63 (Natera's Objections to Report and Recommendation) (attached as Exhibits 1-4); *see also id.*, D.I. 86, 87 (Natera's Renewed Motion to Dismiss) (attached as Exhibits 7-8); *see also id.*, D.I. 100-02, 107-08 (Natera's Motion for Summary Judgment of Invalidity and Briefing Related Thereto) (attached as exhibits 9-13). The two patents asserted in CareDX claim priority to applications filed in 2009 and 2010, which is before the earliest possible priority date for the claims of the '220 Patent.

~~119~~128. Similarly, in *Illumina, Inc. v. Natera, Inc.*, No. 18-cv-01662 (N.D. Cal.) ("Illumina"), Natera has alleged that the claims of U.S. Patent No. 9,493,831 are unpatentable under Section 101. *See Illumina*, No. 18-cv-01662, D.I. 24, 35 (Motion to Dismiss and Briefing Related Thereto) (attached as Exhibits 5-6). The patent asserted in Illumina claims priority to an application filed in 2010, which is before the earliest possible priority date for the claims of the '220 Patent.

120~~0~~9. In this case, representative claim 1 of the '220 Patent recites a "a method for amplifying and sequencing DNA" comprising (1) ligating adaptors to isolated cell-free DNA, (2) performing a first round of polymerase chain reaction (PCR), (3) performing a second, "nested" round of PCR that includes use of a sequencing tag, and (4) performing high-throughput sequencing to sequence the cell-free DNA.

~~121~~130. But in *CareDX*, Natera itself acknowledged that cell-free DNA is a natural phenomenon, and alleged that amplification and sequencing methods, such as PCR and high throughput sequencing, were known and used in the art to detect and sequence cell-free DNA. *E.g., CareDX*, D.I. 10 at 12-19; D.I. 19 at 6-7; D.I. 63 at 3-5. And in *Illumina*, Natera also argued that cell-free DNA is "naturally occurring," and the use of "well-known, routine, and conventional amplification techniques"—including nested PCR, and the use of primers with attached sequencing tags—to amplify and sequence the DNA is not patentable. *See Illumina*, No. 18-cv-01662, D.I. 24 at 2, 6-8; D.I. 35 at 2-9.

~~122~~131. Thus, by Natera's own admissions, the claims of the '220 Patent are unpatentable under 35 U.S.C. § 101, and Natera should never have filed its Complaint against the Counterclaimants.

Invalidity under 35 U.S.C. §§ 102 and 103

~~123~~132. The claims of the '220 Patent are invalid under 35 U.S.C. § 102 and/or § 103, in view of, for example, the following prior art, alone or in combination with additional prior art: Mir, with Siebert, Wang, Spertini, or Makarov, which disclose all elements of the '220 Patent claims. Natera disclosed Mir, Wang, Spertini, and Makarov as four of thousands of references during prosecution of the '220 Patent. Natera did not disclose Siebert to the USPTO during prosecution of the '220 Patent. Moreover, the '220 Patent is at least obvious under 35 U.S.C. § 103 given Natera's own admissions made in court filings in this District and elsewhere, representative examples of which are set forth above in paragraphs ~~117~~126-~~22~~31.

~~124~~133. The '220 Patent is also not entitled to a priority date earlier than its filing date of January 15, 2020, because Natera's provisional applications and earlier-filed applications do not comply with the requirements of 35 U.S.C § 112, as required by 35 U.S.C §§ 119 and 120. The provisional applications and earlier-filed applications do not contain a written description of the claims of the '220 Patent or contain sufficient information to enable a person of ordinary skill in the art to which they pertain to practice the full scope of the claims of the '220 Patent. Indeed, none of the provisional applications or earlier-filed applications disclosed the claimed methods or sought claims corresponding to the claims of the '220 Patent, which recite processes that Natera did not invent.

~~125~~134. Because the '220 Patent is not entitled to a priority date earlier than its filing date of January 15, 2020, it is invalid under 35 U.S.C. § 102 and/or § 103, in further view of, for example, the following prior art, alone or in combination with additional prior art: Hu or Murtaza, which disclose all elements of the '220 Patent claims. Hu and Murtaza were disclosed as two of thousands of references to the USPTO during prosecution of the '220 Patent.

135. The ’220 patent is further invalid for failing to name the proper inventors under 35 U.S.C. § 102(f), as set forth above in paragraphs 354-88 of Defendants’ answer.

Invalidity under 35 U.S.C. § 112 and Improper Inventorship

~~126~~136. The claims of the ’220 Patent are invalid under 35 U.S.C. § 112.

~~127~~137. The claims of the ’220 Patent lack written description support in the specification.

~~128~~138. As an example, the specification of the ’220 Patent does not disclose an embodiment or example corresponding to claim 1 of the ’220 Patent and does not otherwise disclose that the named inventors of the ’220 Patent were in possession of the alleged invention recited in the claims as of the priority date of the ’220 Patent.

~~129~~139. Indeed, prior to the filing of the ’220 Patent application on January 15, 2020, Natera had never disclosed the claimed methods nor sought claims corresponding to the claims of the ’220 Patent.

~~130~~140. The specification also does not contain sufficient information to enable a person of ordinary skill in the art to which the patent pertains to practice the full scope of the claims of the ’220 Patent.

~~131~~141. The ’220 Patent does not satisfy the requirements of 35 U.S.C. § 112 because the applicants for the ’220 Patent did not themselves invent the subject matter sought to be patented—an independent ground for invalidating the patent.

~~ELEVENTH~~FOURTEENTH COUNTERCLAIM
(Declaratory Judgment of Unenforceability Of The ’220 Patent Due to Inequitable Conduct)

~~132~~142. The Counterclaimants reallege and incorporate its preliminary statement, and the

allegations set forth in paragraphs 1-~~131~~141 of these Counterclaims as if fully restated herein.

~~133. The '220 Patent is unenforceable due to Natera's inequitable conduct during the~~

~~prosecution of the '220 Patent.~~

134. On information and belief, Dr. Matthew Rabinowitz is the Executive Chairman, founder, and former CEO of Natera, as well as a named inventor on the '220 Patent. Dr. Rabinowitz had a general duty of candor and good faith in his dealings with the USPTO. Pursuant to 37 C.F.R. § 1.56, an inventor has an affirmative obligation to disclose to the USPTO all information known to be material to the examination of a pending patent application. On January 15, 2020, in connection with the application that led to the '220 Patent, Dr. Rabinowitz filed an Inventor's Oath or Declaration with the USPTO pursuant to 37 C.F.R. § 1.63, acknowledging that he was "aware of the duty to disclose to the Office all information known to the person to be material to patentability."

135. According to Natera's Form 10-Q for the quarterly period ended June 30, 2020 dated August 6, 2020, "Dr. Rabinowitz spends significant time with [Natera] and is active in [Natera's] management." Ex. 14 at 68; *see also id.* at 67-68 ("If we lose the services of our founder and Executive Chairman or other members of our senior management team, we may not be able to execute our business strategy.").

136. On information and belief, as a named inventor on the patents in dispute and the Executive Chairman of Natera and someone active in Natera's management, Dr. Rabinowitz was aware of the ongoing action between Natera and ArcherDX, Inc. captioned *Natera, Inc., v. ArcherDX, Inc.*, No. 1:20-cv-125 (D. Del.), including (1) ArcherDX, Inc.'s Answer filed on March 25, 2020 (D.I. 14) ("Answer"), (2) ArcherDX, Inc.'s Answer to the First Amended Complaint filed on May 13, 2020 (D.I. 21) ("Answer to FAC"), (3) ArcherDX, Inc.'s Opening Brief in Support of its Motion for Judgment on the Pleadings filed on June 4, 2020 (D.I. 24) ("12(c) Motion"), and (4) ArcherDX, Inc.'s Reply Brief in Support of its Motion for Judgment on the Pleadings filed on July 30, 2020 (D.I. 24) ("12(c) Reply"). On information and belief,

by reason of his position as an

inventor and the Executive Chairman of Natera and as someone active in Natera's management, Dr. Rabinowitz knew of the arguments set forth in these filings while the '220 Patent was still in prosecution before the USPTO.

137. ArcherDX, Inc.'s Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply set forth invalidity arguments under 35 U.S.C. §§ 101, 103, and 112 for patents closely related to the Asserted Patent, including U.S. Patent No. 10,538,814 (the "'814 Patent") of which the Asserted Patent is a continuation, and on which Dr. Rabinowitz is also named as an inventor.

138. ArcherDX, Inc.'s Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply set forth arguments that the '814 Patent, which is directed to the same unpatentable matter as the '220 Patent, is not patentable under § 101. For example, they set forth that claims directed to a "method of amplifying and sequencing" cell-free DNA comprising (1) ligating adaptors to cellfree DNA, (2) performing a first round of PCR, (3) performing a second round of nested PCR, and (4) performing high throughput sequencing are directed to unpatentable subject matter. *See* 12(c) Motion at 13-15 ("The asserted claims begin with naturally occurring cfDNA and, after amplification and detection, end with the same genetic information; the purpose of the claim is to detect."); 12(c) Reply at 8; Answer to FAC at Counterclaims ¶¶ 17-22. The Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply set forth that such claims are directed to the natural phenomenon of detecting cell free DNA and utilize well known techniques of amplification and sequencing. *See* 12(c) Motion at 16-19 ("[T]he claims recite the use of generic, well-known elements such as 'primers,' 'adaptors,' and 'sequencing tags' for use in conventional and routine 'PCR' and 'high throughput sequencing.'"); 12(c) Reply

at 9-10; Answer to FAC at Counterclaims ¶¶ 17-22. Further, they highlighted statements made by Natera in other litigation arguing the same.

See 12(c) Motion at 16-18 ("Natera's admissions readily show that each method step was routine."); 12(c) Reply at 9-10; Answer to FAC at ¶ 37.

139. ArcherDX, Inc.'s Answer and Answer to FAC set forth arguments that the '814 Patent, which claims highly similar methods to the '220 Patent, is invalid under § 103. For example, they set forth that the prior art of Mir alone or Mir in a specific combination with Wang, Spertini, or Makarov, discloses all elements of the '814 Patent claims. *See* Answer to FAC at Counterclaims ¶¶ 23-25. The Answer and Answer to FAC also set forth that Mir disclosed the elements that the USPTO's examiner mistakenly stated were not in the prior art, such as, the "amplification of . . . circulating nucleic acids," "sequencing steps, . . . incorporat[ing] a universal or common primer, and . . . a sequencing tag," and "'nested PCR' following the recited 'first PCR of 'cell-free DNA.'" *See id.* at ¶ 37, 44. The Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply also highlighted statements made by Natera in other litigation describing claim elements as routine and conventional and, hence, part of the state of the art and within the person of ordinary skill in the art's skill. *See* 12(c) Motion at 16-18 ("Natera's admissions readily show that each method step was routine."); 12(c) Reply at 9-10; Answer to FAC at ¶ 37.

140. ArcherDX, Inc.'s Answer and Answer to FAC set forth arguments that the '814 Patent is invalid under § 112. For example, they set forth that the '814 Patent, which shares a specification with the '220 Patent, does not disclose (a) an embodiment corresponding to the claimed methods, (b) that the named inventors were in possession of the alleged invention, or (c) sufficient information to enabled a person of ordinary skill in the art to practice the claims.

See Answer to FAC at Counterclaims ¶¶ 26-31. The Answer and Answer to FAC set forth that the claims were not entitled to a priority date earlier than the filing date. *See id.* at Counterclaims ¶ 25.

141. On information and belief, as the Executive Chairman of Natera and someone active in Natera's management, Dr. Rabinowitz was also aware of the ongoing action between Natera and CareDX captioned *CareDX, Inc. et al. v. Natera, Inc.*, No. 19-cv-567 (D. Del.), including (1) Natera's Reply in Support of Motion to Dismiss filed on June 24, 2019 (D.I. 19), (2) Natera's Objections to Report and Recommendations filed on February 24, 2020 (D.I. 63), (3) Natera's Opening Brief in Support of Renewed Motion to Dismiss filed on April 9, 2020 (D.I. 87), (4) Natera's Opening Brief in Support of Summary Judgment of Invalidity filed on June 11, 2020 (D.I. 101), and (5) Natera's Statement re Motion for Summary Judgment of Invalidity filed on June 11, 2020 (D.I. 102) (collectively, "CareDX Briefing"). On information and belief, by reason of his position as the Executive Chairman of Natera and as someone active in Natera's management, Dr. Rabinowitz knew of Natera's own arguments set forth in these filings while the '220 Patent was still in prosecution before the USPTO.

142. Natera's CareDX Briefing sets forth arguments for invalidity under 35 U.S.C. § 101 for patents claiming methods of detecting cell-free DNA, including statements of what was "routine" and "conventional" as of 2009 and 2010, prior to the earliest possible priority date for the claims of the '220 Patent.

143. On information and belief, as the Executive Chairman of Natera and someone active in Natera's management, Dr. Rabinowitz was aware of the action between Natera and Illumina, captioned *Illumina, Inc. v. Natera, Inc.*, No. 18-cv-01662

(N.D. Cal.), including (1) Natera's Motion to Dismiss filed May 17, 2018 (D.I. 24), and (2) Natera's Reply in Support of Motion to Dismiss filed June 7, 2018 (D.I. 35) (collectively, "Illumina Briefing"). On information and belief, by reason of his position as the Executive Chairman of Natera and as

someone active in Natera's management, Dr. Rabinowitz knew of Natera's own arguments set forth in these filings while the '220 Patent was still in prosecution before the USPTO.

144. Natera's Illumina Briefing sets forth arguments for invalidity under 35 U.S.C. § 101 for a patent claiming methods of amplifying and sequencing DNA, including statements of what was "routine" and "conventional" as of 2010, prior to the earliest possible priority date for the claims of the '220 Patent.

145. Despite knowing of the arguments set forth in ArcherDX, Inc.'s Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply, as well as Natera's CareDX Briefing and Natera's Illumina Briefing, Dr. Rabinowitz failed to disclose any of these documents to the USPTO during prosecution of the '220 Patent.

146. Dr. Rabinowitz's failure to disclose these documents to the USPTO was but-for material to the issuance of the '220 Patent. If the USPTO had been made aware of these documents setting forth arguments for invalidity under §§ 101, 103, and 112, the '220 Patent would not have issued.

147. As set forth in the Counterclaimants' Counterclaims filed herewith (¶¶ 117-22), the arguments presented in ArcherDX, Inc.'s Answer, Answer to FAC, 12(c) Motion, and 12(c) Reply, as well as Natera's statements made in the Illumina Briefing and the CareDX Briefing establish that the claims of the '220 Patent are unpatentable under § 101 (and, as detailed below, support a finding that these claims are obvious). For example,

Archer's 12(e) motion includes the following table highlighting Natera's admissions that elements of the '814 Patent, which correspond to elements of the '220 Patent, are routine or conventional:

'814 Claim Language	**Natera Admissions**
1. A method for amplifying and sequencing DNA, comprising:	
ligating adaptors to cell free DNA isolated from a biological sample, wherein the adaptors each comprises a universal priming site;	"The DNA in the sample may have **ligation adapters**... appended, wherein **the ligation adapters contain a universal priming sequence**, followed by a universal amplification... this may be done **using a *standard protocol* designed to create sequencing libraries**." '814 Patent, 94:11-16.
performing a first PCR to simultaneously amplify at least 10 target loci using a universal primer and at least 10 target specific primers in a single reaction volume;	"The specification lists several **well known PCR techniques** that can be used to carry out the claimed method, such as '... **multiplex PCR.**'" Illumina Mot., 7. "**Primers routinely** are used in these amplification methods to bind to the **regions of a DNA strand where the DNA sequences of interest are located.**" Illumina Mot., 7. "Universal amplification of DNA using ligated adaptors **with primers specific to the adaptor tags**,... has the effect of enriching the proportion of shorter DNA strands... [E]xample protocols **are published and well known to those in the art**." '814 Patent, 212:14-21. "In some embodiments [the commercially available] QIAGEN **Multiplex PCR Kit** is used..." '814 Patent, 235:15-16.
performing a second, nested PCR to simultaneously amplify the at least 10 target loci using the universal primer and at least 10 inner target-specific primers in a single reaction volume,	(Same as above) "[R]unning **multiple cycles of amplification** to copy DNA sequences was **routine and conventional**." Illumina Reply, 7. "The specification lists several **well known PCR techniques**... such as... multiplex PCR, or **nested PCR**." Illumina Mot., 7.
wherein at least one of the primers comprises a sequencing tag;	"It is also **routine and conventional** in the art to attach to the primers what are known as **sequence 'tag[s].**'" Illumina Mot., 7.
performing high throughput sequencing to sequence the amplified DNA comprising the target loci.	"[T]he asserted claims recite nothing more than **conventional techniques**, such as... **high throughput sequencing**." CareDX Reply, 6-7.

143. Defendants incorporate herein by reference the facts set forth with particularly in

paragraphs 354-88 of their answer above. As alleged in the incorporated paragraphs, the '220 patent is unenforceable due to inequitable conduct.

If Dr. Rabinowitz had disclosed these documents to the USPTO, the USPTO would not have issued the claims.

148. As set forth in the Counterclaimants' Counterclaims filed herewith (¶¶ 123-25), the arguments presented in ArcherDX's Answer and Answer to FAC establish that the claims of the '220 Patent are invalid as obvious under § 103. For example, ArcherDX, Inc.'s Answer and Answer to the FAC disclose that the elements of the claims of the '220 Patent that the USPTO's examiner concluded were missing from the prior art, namely "multiplex using universal or common primers and a second step of nested amplification on the same multiplex amplified targets," are indeed disclosed in the prior art, including in Mir. ArcherDX, Inc.'s Answer ¶ 131; ArcherDX's Answer to FAC ¶¶ 37, 44. While Natera disclosed Mir to the USPTO, it was buried in thousands of references disclosed during prosecution of the '220 Patent. By way of another example, ArcherDX, Inc.'s Answer and Answer to the FAC highlighted statements made by Natera in other litigations describing elements found in the '220 Patent claims as routine and conventional. Archer DX, Inc.'s Answer ¶ 31; ArcherDX's Answer to FAC ¶¶ 37. ArcherDX, Inc.'s 12(c) Motion and 12(c) Reply further highlight specific admissions by Natera that the elements of the claims of the '220 Patent that the examiner concluded were missing from the prior art were routine and conventional prior to the earliest claimed priority of the '220 Patent. *See* 12(c) Motion at 16-18 ("The specification lists several well-known PCR techniques... such as... nested PCR" and "It is also routine and conventional in the art to attach to the primers what are known as sequence 'tag[s].'"); *see also* 12(c) Reply at 9. If Dr. Rabinowitz had disclosed these documents to the USPTO, the USPTO would not have issued the claims.

149. As set forth in the Counterclaimants' Counterclaims filed herewith (¶¶ 26-31), the arguments presented in ArcherDX, Inc.'s Answer and Answer to FAC establish that the claims of the '220 Patent are invalid under § 112 for lack of written description and enablement. If Dr.

Rabinowitz had disclosed these documents to the USPTO, the USPTO would not have issued the claims.

150. Upon information and belief, Dr. Rabinowitz knew that he had a duty to disclose these documents to the USPTO. Indeed, some litigation documents, including some filings from the Illumina action, were disclosed to the USPTO during prosecution of the '220 Patent. For example, Natera's "Motion to Dismiss" and "Opening Brief in Support of Motion to Dismiss" filed on May 16, 2019, briefing related to its motion to dismiss under 35 U.S.C. § 101, in the Illumina action was disclosed to the USPTO during prosecution. Moreover, Natera's "First Amended Answer, Affirmative Defenses and Counterclaims" filed August 16, 2018, its Answer in the Illumina action, was also disclosed to the USPTO during prosecution. These disclosures show that, as the Executive Chairman of Natera and someone active in Natera's management, Dr. Rabinowitz understood that Answers and briefing related to § 101 motions can be material to patentability and must be disclosed to the USPTO. Despite this, Dr. Rabinowitz failed to disclose any of the documents described above (¶¶ 197-205) that are material to patentability. The single most reasonable inference able to be drawn from these facts is that Dr. Rabinowitz's failure to disclose was the result of a specific intent to deceive the USPTO.

151. Dr. Rabinowitz engaged in inequitable conduct in the prosecution of the '220 Patent. Thus, the '220 Patent is unenforceable.

RESERVATION OF RIGHTS

~~152~~144. The Counterclaimants expressly reserve the right to assert any additional defenses or counterclaims that may now exist or in the future may be available based on discovery and further factual investigation in this case.

DEMAND FOR JURY TRIAL

~~153~~145. The Counterclaimants hereby demand a trial by jury of all issues so triable in this action.

PRAYER FOR RELIEF

~~154~~146. The Counterclaimants respectfully request this Court grant relief as follows:

A. Judgment that Natera's Second Amended Complaint in its entirety be dismissed with prejudice;

B. Judgment that Natera is entitled to nothing by its Second Amended Complaint, including that Natera is not entitled to an award of compensatory damages, attorneys' fees, costs, pre-judgment or post- judgment interest under 35 U.S.C. §§ 284 or 285, or any applicable law;

C. Denial of any and all of Natera's requests for injunctive relief;

D. Judgment that the Counterclaimants have not infringed, and are not infringing, any valid and enforceable claim of the Asserted Patents by its sale of LIQUIDPlex™, FusionPlex®, or VariantPlex® for research use only;

E. Judgment that the claims of the Asserted Patents are invalid;

F. Judgment that Natera and/or any of its successors and attorneys, and all persons in active concert or participation with any of them, are enjoined from directly or indirectly asserting infringement or instituting any further action for infringement of the Asserted Patents against ArcherDX, or any of ArcherDX's customers, end-users, agents, suppliers, contractors, consultants, successors, and assigns;

G. Judgment that the Asserted Patents are unenforceable;

~~G~~H. Order that this case is "exceptional" pursuant to 35 U.S.C. § 285 entitling ArcherDX to an award of its reasonable and necessary attorneys' fees, expenses, and costs, and prejudgment and post-judgment interest thereon;

~~H~~I. Order awarding the Counterclaimants their costs incurred in this action; and

~~I~~J. Grant to the Counterclaimants such other and further relief as the Court deems just and proper.

Dated: ~~February 5~~September 1, 2021

Respectfully submitted,

FARNAN LLP

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Summary report: **Litera® Change-Pro for Word 10.8.2.11 Document comparison done on 9/1/2021 11:31:45 PM**	
Style name: Default Style	
Intelligent Table Comparison: Active	
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Format changes	0
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